SEE PARTIL FOR MANUALLY A SIGNED SIGNATURE PAGE

# FORM 1-A Offering Statement under Regulation A for Cardiomedics, Inc.

UNITED STATES SECURITIES AND EXCHANGE COMMISSION WASHINGTON, DC 20549



REGULATION A OFFERING STATEMENT

**UNDER THE SECURITIES ACT OF 1933** 

Cardiomedics, Inc.
(Exact name of Issuer as specified in its Charter)

Nevada
(State Or Other Jurisdiction Of Incorporation Or Organization)

33-0196206 (IRS Employer Identification No.)

18872 Bardeen Avenue

Irvine, Ca 92612

(Address Of Principal Executive Offices)

Mail Processing Section

MAR 3 1 2009

Marvin P. Loeb, Chairman And Chief Executive Officer Cardiomedics, Inc. 18872 Bardeen Ave. Washington, DC 105

Irvine, Ca 92612
(Name And Address Of Agent For Service)

5900 Industrial Classification No.

1-949-951-3800, Ext. 222 (Telephone Number, Including Area Code, Of Agent For Service)

**COPY TO:** 

J. Holt Smith, Esq.
Smith & Associates
411 Santa Monica Blvd., Suite B
Los Angeles, CA 90401
1-310-656-1000

THIS OFFERING STATEMENT SHALL ONLY BE QUALIFIED UPON AN ORDER OF THE COMISSION, UNLESS A SUBSEQUENT AMENDMENT IS FILED INDICATING THE INTENTION TO BECOME QUALIFIED BY OPERATION OF THE TERMS OF REGULATION A.

lf	any	of the	sec	urities	being	regis	tere	d on	this	Form	are	to be	offere	d on	а
delayed	or	continu	ous	basis	pursu	ıant i	to F	Rule	415	under	the	Secu	ırities	Act	of
1933,che	eck t	he follo	wing	box:	X ·										

If the registration elects to deliver its annual report to security holders, or a complete and legal facsimile thereof pursuant to Item 11(a) (1) of this Form, check the following box:

# CALCULATION OF REGISTRATION FEE

Title of Securities To Be Registered	Amount To Be Registered	Offering Price Per Share (	Aggregate Offering 1) Price (1)	Amount of Registration Fee
	<del></del>			
Shares of Common Stock (\$0.01 Par Value)	5,000,000	\$1.00	\$5,000,000	\$ 0

Approximate date of commencement of proposed sale to the public: \_\_\_\_\_\_, 2009.

<sup>(1)</sup> Estimated solely for the purpose of calculating the registration Fee.

#### PART 1 - NOTIFICATION

# ITEM 1. Significant Parties

The Issuer's officers and directors are as follows:

List the full names and business and residential address, as applicable, for the following persons:

# (a) The Issuer's Directors:

## <u>Name</u>

Marvin P. Loeb, Chairman of Board & CEO

<u>Business Address</u>

25901 Commercentre Dr.

Lake Forest, CA 92630

Lake Forest, CA 92630

John McCallum, President, COO & Director Business Address
18872 Bardeen Ave.
Irvine, CA 92612

Donald Baker, Director Business Address
544 Earlston Road
Kenilworth, IL 60043

Thomas R. Ulie, Director Business Address P.O. Box 814 Mercer Island, WA 98040

Glenn D. Yeik, Director <u>Business Address</u> 25901 Commercentre Dr. Lake Forest, CA 92630

(b) The Issuer's Officers:

Marvin P. Loeb, Chairman of Board & CEO Business Address
25901 Commercentre Dr.
Lake Forest, CA 92630

Residence 5567-A Via Portora Laguna Hills, CA 92637

Residence 1611 A South Melrose Dr., #304 Vista, CA 92081

Residence 544 Earlston Road Kenilworth, IL 60043

Residence P.O. Box 814 Mercer Island, WA 98040

Residence 21831 Eagle Lake Circle Lake Forest, CA 92630

Residence 5567-A Via Portora Laguna Hills, CA 92637 John McCallum, President, COO & Director

**Business Address** 

18872 Bardeen Ave.

Irvine, CA 92612

Residence

1611 A South Melrose Dr., #304

Vista, CA 92081

Robert J. Sullivan, Vice President

**Business Address** 

18872 Bardeen Ave. Irvine, CA 92612

Residence

22825 Islamare Lane Lake Forest, CA 92630

Lorrie L. Stratton, Treasurer & CAO

**Business Address** 

18872 Bardeen Ave.

Irvine, CA 92612

Residence

14701 Danborough Road

Tustin, CA 92780

Alan E. Loeb, Secretary

**Business Address** 

2670 E. Milkyway

Gilbert, AZ 85296

Residence

2670 E. Milkyway Gilbert, AZ 85296

The Issuer's General Partner: (c)

Not applicable. There is no general partner

(d) Record owners of 5 percent or more of any class of the Issuer's equity securities:

The following are of record and beneficial owners of 5% or more of the Issuer's shares of \$0.01 per value common stock (the "Shares") issued and outstanding at the time of filing, the number of shares and the percent of the outstanding:.

Shares Held	Outstanding
4,007,602 816,999	53.8% 11.0%
	4,007,602

Beneficial owners of 5 percent or more of any class of the Issuer's (e) equity securities:

None, other than the persons listed in (d) above.

(f) Promoters of the Issuer:

The promoters of the issuer are:

Marvin P. Loeb, Chairman & CEO John McCallum, President, Director & COO

(g) Affiliates of the Issuer.

Not Applicable. There are none.

(h) Counsel to the Issuer with respect to the proposed offering:

J. Holt Smith, Esq. Smith & Associates 411 Santa Monica Blvd., Suite B Los Angeles, CA 90401 1-310-656-1000

- (i) Each underwriter with respect to the proposed offering: Not Applicable. There are none.
- (j) The underwriter's directors: Not Applicable.
- (k) The underwriter's officers: Not Applicable.
- (I) The underwriter's general partner: and Not Applicable.
- (m) Counsel to the underwriter: Not Applicable.

# ITEM 2. Application of Rule 262

State whether any of the persons identified in response to Item 1 are subject to any of the disqualification provisions set forth in Rule 262.

- (a) Not Applicable. None of the above persons are subject to any of the disqualifications set forth in Rule 262.
- (b) Not applicable.

# ITEM 3. Affiliate Sales

Not applicable. No resale of any outstanding securities of the Issuer held by affiliates are included in this Form 1-A.

- ITEM 4. Jurisdictions in which securities are to be offered.
  - (a) The securities are to be offered by the Issuer and any broker/dealers who enter into Selling Dealer Agreements with the Issuer, if any, and their salespersons, if any.
  - (b) The Offering will be made by coordination in the states whose Blue Sky laws permit registration of securities registered for sale by the Commission by coordination and in such other states as may be requested by broker/dealers who enter into a Selling Dealer Agreement with the Company, if any.
- ITEM 5. Unregistered Securities Issued and Sold Within One Year.
  - (a) The following unregistered securities of the Company were issued and/or sold within one year prior to filing of this Form 1-A.
    - (1) Name of Issuer: Cardiomedics, Inc., a Nevada corporation.
    - (2) Title and Amount of Securities Issued:
      - a. The Company issued 720,000 Shares to its Chairman & CEO in lieu of cash compensation for serving as the Company's Chairman and CEO from January 1, 2006 through December 31, 2008.
      - b. From June 1, 2005 through the date of filing of this Form 1-A, the Company sold in private transactions \$900,000 of 6% Senior, Secured Convertible Notes (the "Notes") to Marvin P. Loeb, the Company's Chairman and CEO, and \$600,000 of Notes to Thomas R. Ulie and \$50,000 to Donald Baker, Directors of the Company. The principal and any accrued interest on the Notes are convertible into Shares of the Company at a conversion price of \$0.50 per Share.
    - (3) Aggregate offering price and basis of Compensation:
      - a. None. No Compensation was paid.
      - b. \$1,000,000 of Convertible Notes. No compensation was paid.

(b) Sales of unregistered securities.

See (2) a and b above.

- (c) Indicate the section of Securities Act or Commission rule or regulation relied upon for exemption from registration requirements.
  - (1) The above issuance and/or sales of securities were made pursuant to Section 4(2) of the Securities Act of 1933, as amended, as transactions not involving a public offering, and the Shares are "restricted" pursuant to Rule 144.
  - (2) None of the officers, directors or principal securities holders of the Company have sold any securities of the Company within the twelve (12) months prior to filing of this Form 1-A.

# ITEM 6. Other Present or Proposed Offerings

If permissible, the Company plans to offer privately, pursuant to Regulation D of the Securities Act of 1933, as amended, securities of the same class (\$0.01 par value common stock), at the same price as the Shares offered hereby, solely to Accredited Investors in those States whose Blue Sky Laws do not permit registration of this Offering under Regulation A. In any event, the gross proceeds from sales of securities under both of said offerings under Regulations D and A shall not exceed \$5,000,000, and the Private Offering Memorandum of the Regulation D Offering will contain exactly the same risk factors, disclosures, descriptions, tables and financial information as the Form 1-A Offering Circular. Please advise us if this is not permissible. If not permissible, we will not offer any Shares pursuant to Regulation D.

# ITEM 7. Marketing Arrangements

- (a) Not Applicable. There are no marketing arrangements in place with any broker/dealers.
- (b) Not Applicable. There are no marketing arrangements in place with any broker/dealers.
- ITEM 8. Relationship with Issuer of Experts Named in the Offering Statement.

Not Applicable.

ITEM 9. Use of a Solicitation of Interest Document.

Not Applicable. No written documents or broadcast scripts were used prior to the filing of this notification and none will be used prior to its qualification by the Commission.

(vii)

# CARDIOMEDICS, INC.

# **CROSS REFERENCE SHEET**

<u>ltem i</u>	n Form 1-A	Location in Offering Circular
1.	Cover Page of Offering Circular	Cover Page of Offering Circular
2.	Distribution Spread	Cover Page of Offering Circular
3.	Summary Information, Risk Factors and Dilution	Summary; Risk Factors; Dilution
4.	Plan of Distribution	The Offering
5.	Use of Proceeds by Issuer	Use of Proceeds
6.	Description of Business	The Company and Business
7.	Description of property	Business – Properties
8.	Directors, Executive Officers and Significant Employees	Management
9.	Remuneration of Directors and Officers	Management – Compensation
10.	Security Ownership of Management and and Certain Security Holders	Security Ownership of Management and Certain Control Holders
11.	Interest of Management and Others in Certain Management Transactions	Transactions with Management
12.	Securities Being Offered	Description of Securities

#### **PART II**

# PRELIMINARY OFFERING CIRCULAR DATED SUBJECT TO COMPLETION

2009

CARDIOMEDICS, INC.

Up to \$5,000,000

# 5,000,000 SHARES OF COMMON STOCK AT A PRICE OF \$1.00 PER SHARE

The Date of This Offering	Circ	ular is _				_, 200	9		
Approximate Date of Commencement	ent of	Sale to	the P	ublic	:			, 2	009
						_	_		_

CARDIOMEDICS, INC., a Nevada corporation (hereinafter referred to as "we", "our," "us" or the "Company"), is offering up to 5,000,000 shares of its \$0.01 par value common stock (the "Shares") to the public at a price of \$1.00 per Share for an aggregate of \$5,000,000 (the "Offering").

This Offering is being made on a "best efforts" basis pursuant to Section 3(b) of the Securities Act of 1933, as amended (the "Act") by the Company and by such Broker/Dealers who may enter into Selling Dealer Agreements with us, if any. We are presently privately held, and there is presently no public trading market for our Shares. Although the Shares sold pursuant to this Offering Circular, when issued, will be fully paid, non-assessable and freely tradable, without any legend restricting transfers, we cannot assure that any public trading market in our Shares will arise. We plan to use the stock symbol "CDMX", if available, in the event a public trading market in our Shares arises.

There is no minimum number of Shares which must be sold to complete this Offering. The proceeds of sales of Shares will not be deposited into an escrow account, and the net proceeds of the sales of Shares will be immediately delivered to and available for use by the Company. We can give no assurance that any or all of the Shares being offered will be sold.

This Offering of Shares will terminate on the earlier to occur of the sale of all of the 5,000,000 Shares being offered or 180 days following the qualification date of this Offering Circular, unless the offering period is extended without notice by the Company for an additional 120 days.

THIS OFFERING CIRCULAR SHALL ONLY BE QUALIFIED UPON THE ORDER OF THE COMMISSION. UNLESS A SUBSEQUENT AMENDMENT IF FILED INDICATING THE INTENTION TO BECOME QUALIFIED BY OPERATION OF **REGULATION A.** 

Within 60 days after the closing date of the Offering, the Company will issue at no cost to the purchasers of Shares in this Offering, one-half Class A Warrant for each Share purchased and one-half Class B Warrant for each Share purchased in the Offering. Two (2) Class A Warrants may be exercised to purchase one (1) Share at a price of \$1.50 at any time during a period of six (6) months, commencing twelve (12) months after the closing date of this Offering. Two (2) Class B Warrants may be exercised to purchase one (1) Share at a price of \$2.00 at any time during a period of twelve (12) months, commencing twelve (12) months after the closing date of this Offering. The Warrants will contain no anti-dilution provisions and are redeemable by the Company if the Shares trade at a price at least 50% higher than their respective exercise prices during their respective exercise periods (See "THE OFFERING & PLAN OF DISTRIBUTION").

The Class A and B Warrants and the Shares issuable upon exercise of the Class A and B Warrants are not being registered in the Registration Statement of which this Offering Circular is a part. As a result, no market for the Class A or B Warrants is expected to arise. Shares purchased by the exercise of the Class A and B Warrants, if any, may be sold publicly pursuant to Rule 144 of the Securities and Exchange Commission after six (6) months by holders who are not officers, directors or five percent (5%) owners of the Company's Shares. Officers, directors and 5% owners of the Company's Shares may sell Shares purchased by the exercise of the Class A or B Warrants, if any, publicly pursuant to Rule 144 after six (6) months, subject to certain volume limitations (See "THE OFFERING & PLAN OF DISTRIBUTION").

THESE SECURITIES ARE SPECULATIVE AND INVOLVE A HIGH DEGREE OF RISK. SEE "RISK FACTORS."

INVESTMENT IN SMALL BUSINESSES INVOLVES A HIGH DEGREE OF RISK, AND INVESTORS SHOULD NOT INVEST ANY FUNDS IN THIS OFFERING UNLESS THEY CAN AFFORD TO LOSE THEIR ENTIRE INVESTMENT. SEE THE RISK FACTORS THAT MANAGEMENT BELIEVES PRESENT THE MOST SUBSTANTIAL RISKS TO AN INVESTOR IN THIS OFFERING.

IN MAKING AN INVESTMENT DECISION, INVESTORS MUST RELY UPON THEIR OWN EXAMINATION OF THE ISSUER AND THE TERMS OF THE OFFERING, INCLUDING THE MERITS AND RISKS INVOLVED. THESE SECURITIES HAVE NOT BEEN RECOMMENDED OR APPROVED BY ANY FEDERAL OR STATE SECURITIES COMMISSION OR REGULATORY AUTHORITY. FURTHERMORE, THESE AHTHORITIES HAVE NOT PASSED UPON THE ACCURACY OR ADEQUACY OF THIS DOCUMENT. ANY REPRESENTATION TO THE CONTRARY IS A CRIMINAL OFFENSE.

THE U.S. SECURITIES AND EXCHANGE COMMISSION DOES NOT PASS UPON THE MERITS OF OR GIVE ITS APPROVAL TO ANY OF THE SECURITIES BEING OFFERED OR THE TERMS OF THE OFFERING, NOR DOES IT PASS UPON THE ACCURACY OR COMPLETENESS OF ANY OFFERING CIRCULAR OR OTHER SELLING LITERATURE. THESE SECURITIES ARE OFFERED UNDER AN EXEMPTION FROM REGISTRATION. HOWEVER, THE COMMISSION HAS NOT MADE AN INDEPENDENT DETERMINATION THAT THESE SECURITIES ARE EXEMPT FROM REGISTRATION.

	Price to Public	Commissions	The Company's Net Proceeds <sup>1</sup>
Per Share	\$1.00	\$0.10	\$0.90
Total	\$5,000,000	\$500,000	\$4,500,000 <sup>1</sup>

Assumes all the Shares being offered are sold by broker/dealers who have entered into Selling Dealer Agreements with the Company. This figure represents the estimated net proceeds to the Company, assuming all of the 5,000,000 Shares being offered are sold, before paying the other expenses of the Offering, which are estimated at \$100,000. For a description of the use of the net proceeds of the Offering, see the section titled "USE OF PROCEEDS."

We will pay Broker/Dealers who enter into Selling Dealer Agreements with us, if any, a commission of ten percent (10%) of the gross proceeds of the Shares sold by them, if any. In addition, we will issue to any such Broker/Dealers warrants, exercisable to purchase Shares at a price of \$1.10 per Share during a period of two (2) years, commencing one (1) year following the closing date of this Offering, in an amount equal to ten percent (10%) of the number of Shares sold by them in this Offering, if any. The above mentioned warrants and the Shares underlying such warrants are not included in the Registration Statement of which this Offering Circular is a part (See "THE OFFERING & PLAN OF DISTRIBUTION").

We plan to furnish annual reports to our shareholders, which may include audited or un-audited annual financial statements, or we may post them on our website, www.Cardiomedics.com. If prepared, we may also provide un-audited quarterly financial statements and periodic progress reports to shareholders or post them on our website. We are presently not a reporting company under the Securities Exchange Act of 1934, as amended (the "Exchange Act").

HIS OFFEERING CIRCULAR CONTAINS ALL OF THE REPRESENTATIONS BY THE COMPANY CONCERNING THIS OFFERING, AND NO PERSON SHALL MAKE DIFFERENT OR BROADER STATEMENTS THAN THOSE CONTAINED HEREIN. INVESTORS ARE CAUTIONED NOT TO RELY UPON ANY INFORMATION NOT EXPRESSLY SET FORTH IN THIS OFFERING CIRCULAR.

## **TABLE OF CONTENTS**

TOPIC	PAGE NO
SUMMARY	4
RISK FACTORS	6
FORWARD-LOOKING STATEMENTS	12
CAPITALIZATION	12
DILUTION	13
USE OF PROCEEDS	13
THE OFFERING & PLAN OF DISTRIBUTION	14
THE COMPANY	15
MANAGEMENT'S DISCUSSION AND ANALYSIS	18
BUSINESS	22
MANAGEMENT	32
TRANSACTIONS WITH MANAGEMENT	36
DESCRIPTION OF SECURITIES	38
THE COMMISION'S POLICY ON INDEMNIFICATION	38
SHARES AVAILABLE FOR FUTURE SALE	38
TAX CONSEQUENCES	38
LEGAL MATTERS	38
AVAILABLE INFORMATION	39
FINANCIAL STATEMENTS	39
INDEX TO FINANCIAL STATEMENTS	39
NOTES TO FINANCIAL STATEMENTS	F-5

#### SUMMARY

The following summary is qualified in its entirety by the more detailed information and the financial statements appearing elsewhere in this Offering Circular.

## The Company

Cardiomedics, Inc. ("we", "our," "us" or the "Company") was incorporated under the laws of the State of Nevada on August 25, 1986. Our office and factory is located at 18872 Bardeen Avenue, Irvine, CA 92612. Our telephone number is 1-949-863-2500, our toll free telephone number is 1-888-849-0200, and our President, John McCallum, can be contacted at 1-949-863-2500, Extension 106.

We are engaged in the development, manufacturing, marketing, sale, rental and operation of our (a) CardiAssist™ External Counter Pulsation or "ECP" Systems to treat angina pectoris ("Angina") and Angina patients who also suffer from congestive heart failure ("Heart Failure"), (b) CardiAssess® Cardio Pulmonary Diagnostic or "CPD" Systems to assess the cardiopulmonary condition of Heart Failure patients and evaluate the effect of various therapies, including ECP, pacemakers and drugs, and (c) Cardiomedics® Sleep Disorder Diagnostic or "SDD" Systems to diagnose and evaluate therapies to treat sleep disorders which, if not treated, can cause the patient's cardiac conditions to worsen. We also plan to distribute and market other products in the cardiovascular and pulmonary fields of medicine that can be sold to the same types of customers (physicians, group practices, clinics and hospitals) to whom we sell and rent our current products (See"THE COMPANY" and "BUSINESS".)

All of the above products have been cleared for sale in the United States by the U.S. Food and Drug Administration ("FDA"), and all have been granted the CE Mark for marketing in the European Union. The use of all of these products is covered by and eligible for reimbursement by Medicare, the agency of the U.S. Government that provides health care for approximately 40 million seniors in the United States, and are reimbursed by most insurance companies and health management organizations ("HMOs") in the United States (See "Government Regulation" and "Reimbursement" under "BUSINESS").

Our ECP Systems are the only ECP devices which have been shown in clinical studies, published in peer-reviewed medical journals to produce the following clinical (therapeutic) benefits:

- (a) Reduce mortality in the treatment of Stable (chronic) Heart Failure to 1.85% in the year following 35 hours of ECP therapy, a 90% reduction from the American Heart Association's published figure of 19.1% mortality from Stable Heart Failure (a savings of 17 lives per hundred ECP treated patients), and reduce hospitalizations in the year following 35 hours of ECP therapy to an average of 0.35 hospital admissions, an 87.5% reduction from an average of 2.8 hospital admissions in the year prior to the ECP therapy. An estimated 4 million people in the United States suffer from Heart Failure, and the treatment of Heart Failure is Medicare's largest single cost at about \$40 billion per year.
- (b) Reduce Angina (severe chest pain) attacks by 76%, reduce nitroglycerine (a vasodilator drug for relieving chest pain) by 77% and hospital admissions by 90% in the six month period following 35 hours of ECP therapy, compared to the six months prior to the ECP therapy. An estimated 6 million people in the United States suffer from Angina, and Angina is a major cause of emergency room visits and hospitalization at significant cost to Medicare.
- (c) Reduce mortality from the most common type of Heart Attack in the ECP Group to 6.5% following 4 hours of ECP, a 56% reduction from mortality of 14.7% in the Control Group, during the hospital stay (a savings of 8 lives per hundred ECP treated patients), and the ECP treated patients had 65% fewer progressions to Heart Failure and 35% less residual (recurring) chest pain.

Approximately 1 million Heart Attacks occur each year in the United States, about 25% die before reaching a hospital and about 25% die while hospitalized, a major cost to Medicare.

(d) Increase survival from Cardiogenic Shock (the most serious complication of a Heart Attack) to 35%, a 233% increase from the typical survival of 15% (a savings of 20 lives per hundred ECP treated patients).

(See "Results of Clinical Studies" and "Medicare Reimbursement for ECP Therapy" under "BUSINESS").

Medicare covers the use of our ECP System in the treatment of severe Stable (chronic) Angina patients who are not amenable to (suitable for) balloon angioplasty or bypass surgery, but our ECP System is not presently covered by Medicare for the treatment of less severe Angina, Heart Failure or Heart Attacks. We must successfully conduct a larger clinical study of our ECP System in the treatment of Heart Failure and Angina and a new clinical study in the treatment of Heart Attacks before we can apply for Medicare coverage for these conditions, which we cannot assure will be granted (See "Medicare Reimbursement for ECP" under 'BUSINESS").

Physicians and group practices in the United States and overseas are reluctant to buy expensive equipment for use in their offices, such as our ECP Systems at up to \$100,000, our CPD Systems at up to \$30,000 or our SDD Systems at up to \$120,000, as they normally do not buy expensive equipment for their offices and typically send patients to hospitals for treatment or diagnosis. If they could rent equipment for their office and pay a fee per hour or test, without having to buy the equipment or sign a long term lease, they could earn the fees others charge for these services.

Clinics and hospitals are also reluctant to buy expensive equipment, as they typically have limited capital equipment funds, particularly in the present recession, in which credit lines are being curtailed or cancelled. If they could rent our products and pay a per hour or per test change, without having to buy the equipment or sign a long term lease, they can increase the therapies and diagnostic services they can offer and increase their revenues.

While we will continue to sell our products, our principal efforts in the future are expected to be devoted to renting our products to physicians, group practices, clinics and hospitals for a per hour or per test charge and, in some instances, providing trained nurses or technicians to operate them at a higher per hour or per test charge. Outside the United States, we plan to sell and rent our products for a per hour or per test charge, through distributors to such parties, but without providing nurses & technicians to operate them (See "Per Hour and Per Test Rental Programs" under "BUSINESS").

We had a loss (unaudited) of \$189,371 or \$0.03 per Share on revenues of \$1,142,289 in the calendar year ended December 31, 2008, compared to a loss (unaudited) of \$373,060 or \$0.05 per Share on revenues of \$860,282 in the calendar year ended December 31, 2007. (See "RISK FACTORS," "THE COMPANY," "BUSINESS," "MANAGEMENT'S DISCUSSION AND ANALYSIS" and "FINANCIAL STATEMENTS").

#### The Offering

This Offering Circular covers the offer and sale of up to 5,000,000 of our Shares to the public on a "best efforts" basis by the Company at a price of \$1.00 per share for an aggregate of up to \$5,000,000. There will be no escrow of funds, there is no minimum number of Shares which must be sold to complete this Offering, the net proceeds of sales of Shares will be delivered to and immediately available for use by the Company, and there is no assurance any or all of the Shares being offered will be sold. If less than all of the Shares being offered are sold, the aggregate proceeds may not be sufficient for our immediate and future needs. Purchasers of the Shares being offered by this Offering Circular will suffer immediate and substantial dilution (See "RISK FACTORS", "DILUTION", 'BUSINESS" and "THE OFFERING").

Number of Shares Outstanding Before this Offering: 7,427,060 (11,166,960 on a fully diluted basis).

Number of Shares Outstanding After this Offering: 12,427,060\* (16,166,960\* on a fully diluted basis), assuming all the Shares being offered are sold.

Percentage of Shares Owned by Current Investors after this Offering: 60% (69% on a fully diluted basis), assuming all the Shares being offered are sold.

We will pay Broker/Dealers who enter into Selling Dealer Agreements with us, if any, a commission of up to ten percent (10%) of the gross proceeds from the sales of Shares in this Offering. We will also issue to such Broker Dealers warrants, exercisable for a period of two (2) years, commencing one (1) year from the closing date of this Offering, to purchase Shares at a price of \$1.10 per Share, in an amount up to ten percent (10%) of the number of Shares sold by them in this Offering, if any.

#### **RISK FACTORS**

The Shares being offered are highly speculative, involve a high degree of risk and should be purchased only by parties who can afford to lose the entire amount they invest in the Company. Prospective investors should carefully consider the risks and uncertainties described below and the other information contained in this Offering Circular. The risks described below may not be the only risks we face. This Offering Circular contains forward-looking statements, and our actual results may differ materially from those described herein, (See "FORWARD LOOKING STATEMENTS").

If any of the following risks actually occur, our business, financial condition, results of operations and ability to continue in business could be materially adversely affected. In this event, the market price of our Shares, if any, could decline and you may lose all or part of your investment.

# 1. No Market for our Shares.

We are privately held, and we can give no assurance that a public trading market for our Shares will arise following the closing of this Offering. After completion of this Offering, if a trading market in our Shares arises, the volume of Shares traded may be small, and the investors in this Offering may be unable to liquidate their investment in the Company (See "THE OFFERING & PLAN OF DISTRIBUTION").

# 2. Investors in this Offering Will Suffer Significant Dilution.

Investors purchasing Shares in this Offering will experience significant, immediate dilution of their interest in the Company. At December 31, 2008, our net tangible book value was (\$0.15) per Share. If all of the Shares being offered are sold, our net tangible book value will be \$0.26 per Share, a decrease of \$0.74 per Share to purchasers of the Shares being offered and an increase of \$0.41 per Share at no cost to our present shareholders. (See "DILUTION" and "CAPITALIZATION").

# 3. Risks of a Best Efforts Offering

This Offering is being made by the Company on a "best efforts" basis, and we cannot assure that any or all of the Shares being offered will be sold. The investors in this Offering will not have the benefit of an underwriter passing upon the merits of the Company and this Offering. If less than all of the Shares being offered are sold, the proceeds may be insufficient to meet our immediate and future needs. If we need additional financing, it may not be available to us on acceptable terms or at all, in which case our ability to continue in business will be jeopardized (See "THE OFFERING & PLAN OF DISTRIBUTION", "THE COMPANY" and "BUSINESS").

# 4. Arbitrary Determination of Offering Price

The offering price of our Shares was arbitrarily determined by the Company and is not based on any recognized criteria of value (See "THE OFFERING" and "BUSINESS").

#### 5. No Escrow of Funds

There will be no escrow of the proceeds from the sales of Shares in this Offering, and the net proceeds received from the sales of Shares will be delivered to and immediately available for use by the Company (See "THE OFFERING").

# 6. We Have Had Losses In The Last Two Years and Have Limited Cash Resources

On December 31, 2008, we had \$117,105 of cash and cash equivalents and, along with other assets, we had total current assets of \$498,994 on that date (unaudited). However, on that date, we had accounts payable and accrued expenses of \$478,538 (unaudited). Unless our revenues continue to increase, we are able to collect a significant portion of our accounts receivable, sell most of our goods in inventory to pay our accounts payable, our accrued expenses and finance our operations, we will not be able to operate profitably in the future. If a substantial portion of the Shares being offered are not sold, we may need additional financing in order to remain in business, which financing may not be available to us on acceptable terms or at all, in which case our ability to continue in business will be jeopardized. (See "MANAGEMENTS DISCUSSION AND ANALYSIS", "BUSINESS" and "FINANCIAL STATEMENTS").

## 7. Current Worldwide Recession Could Impact Sales and Rentals

In a severe recession, especially one in which individual wealth is adversely affected by a decline in the market prices of property and investments, the gross national product declines, the viability of banks and financial institutions are in doubt, credit lines may be curtailed, layoffs become common and people put-off expenditures, including expenditures for healthcare, even those which treat serious cardiac conditions. We expect our sales of devices will be adversely affected by such economic conditions, and we are already experiencing delays in orders by some of our customers. While renting devices for a per hour or per test fee may be attractive in such an economic climate, we may not be able to raise sufficient capital to continue our rental program. The effect on us, if the current economic condition becomes more severe or is prolonged, it could materially adversely affect our revenues, financial condition and ability to remain in business (See "BUSINESS").

#### 8. Economic Conditions

If current economic conditions worsen or persist, the sales prices of our products, the per hour and per test charges and the minimum monthly requirements under our Rental Agreements may all have to be lowered, reducing our profit margins and our ability to operate profitably and jeopardizing our remaining in business (See 'BUSINESS").

# 9. Lag in Production of New ECP System Could Adversely Affect Financial Results

There is likely to be a lag between our running-out of our present ECP System model to sell, and the inception of marketing a new model ECP System. We ceased manufacturing our present ECP System in March 2009, because we feared ordering components with long lead times would leave us with an unsold inventory of finished devices or components that we would have to sell at a discount or write-off. Also a software component of our present ECP System is no longer available, and efforts to duplicate it might not be successful. We anticipate the period during which we will have no ECP Systems to sell could last through June 2009 and, perhaps, longer, which will adversely affect our revenues and result in a loss in the quarter ended June 30, 2009. If any unforeseen problem arises and the introduction of the new model ECP System

is delayed, our revenues will be further depressed, our operating loss will be significantly increased and our ability to continue in business will be jeopardized.

# 10. There Are Warrants, Stock Options And Convertible Notes Outstanding and Anti-Dilution Rights That Will Dilute Your Ownership

At December 31, 2008, we had Warrants outstanding to purchase 536,900 Shares at a price of \$3.75 per Share, stock options outstanding under our Incentive and Non-Qualified Stock Option Plans ("Option Plans") to our officers, directors, employees and consultants to purchase an aggregate of 1,088,000 Shares at exercise prices of \$2.35 to \$2.50 per Share, with a weighted average exercise price of \$2.48 per Share, of which options to purchase an aggregate of 603,000 Shares were exercisable on that date. We are also able to grant additional options under our Option Plans in the future. At December 31, 2008, we had \$1,000,000 of 6% Senior, Secured, Convertible Notes outstanding which, with accrued interest, are convertible into Shares at a price of \$0.50 per Share at any time prior to their maturity in 2010, 2011, 2012 and 2013, respectively. Any exercise of these Warrants and Options and any conversion of these Notes and accrued interest will dilute your percentage of ownership in the Company. We may also be required to issue a presently undeterminable number of Shares pursuant to the anti-dilution provisions of our presently outstanding Convertible Notes. The issuance of any such Shares will dilute your percentage of ownership in our Company (See "DILUTION", "CAPITALIZATION", "SECURITIES AUTHORIZED FOR ISSUANCE UNDER EQUITY COMPENSATION PLANS," "DESCRIPTION OF SECURITIES" and "FINANCIAL STATEMENTS").

# 11. We May Issue Preferred Stock That Could Dilute the Holders of Our Shares

We are authorized to issue 1,000,000 shares of Preferred Stock, none of which have been issued to date. Our Board of Directors has broad powers to fix the rights and preferences of any Preferred Stock we may issue, without requiring shareholder approval. The issuance of any of our authorized but unissued Preferred Stock could dilute your percentage of ownership in the Company and have an adverse effect on the rights of the holders of our Shares. (See "DESCRIPTION OF SECURITIES").

## 12. We May Acquire Other Entities

While we presently have no plans to do so, we may engage in acquisitions of other companies and businesses and may use our cash reserves, authorized but unissued Shares or shares of our Preferred Stock to acquire these entities. If we use cash to make acquisitions, our cash reserves may be depleted. If we use our Shares or shares of our Preferred Stock for acquisitions, this will result in a dilution of the percentage of your ownership of our Company. In addition, any acquisitions we might make may involve speculative and risky undertakings. Under Nevada law, acquisitions do not require shareholder approval, except when accomplished by merger or consolidation (See "DESCRIPTION OF SECURITIES").

## 13. Our Stock Price May Be Volatile

The market prices for securities of medical device companies have been volatile. If any public trading market for our Shares arises, it is likely that the future price of our Shares will fluctuate. Many factors can adversely or positively affect the market price of our Shares, such as announcements of sales, earnings or losses, clinical trial results, FDA actions on applications for clearances, approvals or recalls of products, the issuance or acquisition of patents or proprietary rights, lawsuits, recommendations by securities analysts and market conditions in general. The market price of our Shares could also be adversely affected by future issuances of our Shares or shares of our Preferred Stock (see "THE COMPANY" and "BUSINESS").

## 14. Special Risks of Our Business and The Risks of Small Businesses in the Medical Technology Field.

We have found it difficult to sell or lease our present products to physicians or group practices, as physicians are generally unwilling to buy or lease expensive pieces of equipment for use in their offices.

Hospitals and clinics are also reluctant to buy or lease expensive pieces of equipment, as they generally have limited capital equipment budgets. We cannot assure that we will be able to successfully rent our products to physicians, group practices, clinics or hospitals and operate them for some of such parties on their premises or that the revenues from the per hour or per test rental charges will be sufficient to offset our costs, which could adversely affect our ability to remain in business. Small companies in the medical technology field face significant risks, problems, delays, expenses and difficulties in developing, manufacturing, distributing, selling and marketing new medical technologies, especially in view of the significant competition that we have and will continue to encounter in this field (See "THE COMPANY" and "BUSINESS").

# 15. Risks of Premature Cancellation of Rental Agreements.

Our Rental Agreements require the renter to pay us minimum monthly rental charges of up to \$5,600 per month for ECP Systems, up to \$2,400 per month for our CPD Systems or up to \$10,000 per month for our SDD Systems, if we provide the operator of which Systems, over a period of five (5) years, which minimums include our providing, at our expense, parts to provide defective parts of the Systems and preventative maintenance services. Also, in many cases, at the above minimums, we provide a trained nurse or technician to operate the ECP and CPD Systems and a trained sleep technician to operate the SDD Systems. If we do not provide an operator, the minimum monthly rental charges will reflect the absence of this cost. To make these Rental Agreements acceptable to physicians, group practices, clinics and hospitals, the Rental Agreements can be cancelled by the physician, group practice, clinic or hospital on two (2) or three (3) months prior written notice. We cannot assure that a substantial number of our Rental Agreements will not be prematurely cancelled and the Systems returned to us. If we cannot sell or rent a sufficient number of the returned Systems to other physicians, group practices, clinics or hospitals, our working capital may be impaired and our ability to continue in business will be jeopardized (See "THE COMPANY" and "Per Hour and Per Test Rental Program" and "Medicare Reimbursement" under 'BUSINESS").

# 16. We May Need Substantial Additional Financing

Even if all of the Shares being offered are sold, unless our revenues continue at the current level or increase in the near future in an amount exceeding our costs of manufacturing, selling, operations and overhead we may need to raise additional capital, which may not be available to us at an acceptable cost or at all. If such financing is not available, we may not be able to continue in business. Sources of financing may include the sale of additional equity securities, the sale of debt securities, borrowings or the sale or licensing of patent rights (See "THE COMPANY" and "BUSINESS").

## 17. Risks of Borrowing

We issued \$1,000,000 of 6% Senior, Secured Convertible Notes ("Notes") due in 2010 through 2013, which we must pay with accrued interest when due, unless any of the same are converted into Shares, which we cannot assure. We may need to raise additional money to finance the rental of our products to physicians, group practices, clinics and hospitals under Rental Agreements for per hour or per test rental charges and to pay the prime and interest on the Notes. While we presently have no arrangements to borrow from any lenders, if we do, in addition to the expense of interest over the term of the borrowings, any borrowings we undertake will place the assets of our Company at risk. If we are not able to operate profitably in the future or, if the number of cancellations of our Rental Agreements and the return of products exceeds our ability to promptly rent or sell the returned products to others, we may be unable to meet our interest and principal payments due on borrowings or the Notes. A default in any borrowings we may undertake or the Notes may result in the loss of part or all of our assets and may make it impossible for us to remain in business (See "THE COMPANY" and "Per Hour and Per Test Rental Programs" and "Medicare Reimbursement" under "BUSINESS").

## 18. Competition

The medical device business is intensely competitive, and we face competition from both large and small companies, most of whom have greater financial resources and larger management, manufacturing, R & D, marketing, accounting and sales staffs than us, which could adversely affect our ability to compete in this industry (See "Competition" under "BUSINESS").

# 19. We May Not Be Able Adjust To Rapid Technological Changes

We are engaged in an industry in which rapid technological advances are made. There is no assurance that our present products may not face technological obsolescence, we will be able to develop, acquire distribution rights to or licenses for, or obtain regulatory approvals to market new products or keep pace with technological advances by our competitors, which could jeopardize our ability to remain in business (See "THE COMPANY" and "BUSINESS").

# 20. Risks of Developing and Marketing New Products

Developing new medical products entails considerable risk and cost. While we have experience in developing, manufacturing and obtaining FDA clearances for our current products, we cannot assure that we can successfully sell, lease or rent and operate them or acquire, develop or market any new products. If we cannot do so, our ability to remain in business will be jeopardized (See "THE COMPANY" and "BUSINESS").

# 21. Dependence on Key Personnel

The loss of our Chairman & CEO, President & COO, Vice President – Manufacturing or Treasurer & Chief Accounting Officer will have a material adverse effect on our business. Finding replacements for experienced, capable executives in the medical device field is difficult, as there is significant competition for competent executive managers from both large and small companies in this industry (See "MANAGEMENT" and "Personnel" under "BUSINESS").

# 22. We Are Subject To Extensive Government Regulation

Our business is subject to extensive regulation by the FDA and comparable regulatory authorities of foreign countries. Compliance with regulatory requirements and obtaining approvals to test or market new medical devices is expensive and time consuming. We cannot assure that we will be able to continue to meet all regulatory requirements of the FDA and comparable foreign governmental authorities necessary to market our present products or obtain and maintain approvals to test and market any new products. Failing to meet necessary FDA and other governmental requirements will jeopardize our ability to continue in business (See "Government Regulation" under "BUSINESS").

## 23. Clinical Study Uncertainty

We plan to spend up to \$1 million over the next two years on two clinical studies, one of which is a two year, randomized, controlled clinical study of our ECP and CPD Systems in the treatment of Stable (chronic) Heart Failure, and the other is a one year randomized clinical study of our ECP System in the treatment of Acute Heart Failure. We plan to use up to \$500,000 from the net proceeds of sales of the Shares for these studies in 2009 and 2010, if at least \$2.5 million of Shares are sold, which we cannot assure. We also cannot assure that our revenues in 2009 and 2010 will exceed our costs of operations and enable us to finance the balance of the cost of the study, the results of the clinical study will be comparable to the successful results of our earlier clinical study of our ECP System in the treatment of Heart Failure or the study, if successful, will result in Medicare coverage and reimbursement (See "USE OF PROCEEDS", "THE COMPANY" and "Results of Clinical Studies" and "Medicare Reimbursement" under "BUSINESS").

# 24. Risks and Limitations Entailed in Medicare Reimbursement

While our current products are eligible for reimbursement by Medicare and most insurance companies and HMOs, reimbursement of our ECP Systems is limited by Medicare to a small percentage of Angina patients, and its use in the treatment of Heart Failure, the largest potential market for our ECP Systems, is not reimbursed by Medicare. Even if we conduct the two, proposed clinical studies of our ECP System in the treatment of Heart Failure, which will entail up to \$1 million of cost, there is no assurance the results will show our ECP System is beneficial or cost effective, that Medicare and others will grant coverage for the use of these devices or the amount of reimbursement will be sufficient to attract physicians, group practices, clinics or hospitals to buy or rent our ECP Systems. Insurance companies and HMOs tend to follow Medicare's coverage and reimbursement decisions. Failure to obtain or maintain any coverages for our products or obtain sufficient reimbursement amounts could adversely affect our ability to remain in business (See "THE COMPANY" and "Results of Clinical Studies" and "Medicare Reimbursement" under "BUSINESS").

# 25. We Carry Limited Liability Insurance

We carry an aggregate of \$5,000,000 of general liability insurance, including \$5,000,000 of product liability coverage per incident and in the aggregate. We cannot assure that we will be able to maintain this insurance in force at an acceptable cost or that the amount of this insurance will be sufficient to protect our assets in the event of claims by users of our products, patients or other parties. If court awards exceeding the amount of our insurance were made, our assets could be depleted and we may not be able to continue in business (See "Insurance" under "BUSINESS").

# 26. We Are Dependent Upon Obtaining and Maintaining Valid Patents And Licenses

While U.S. Patent No. 7,244,225, covering our Graduated™ Low Pressure ECP Regimen to treat Stable Heart Failure and other medical conditions and improvements to our ECP System, was issued to us on July 17, 2007, and another U.S. Patent, covering an advanced, Graduated™ Low Pressure ECP Regimen to treat Stable Heart Failure, has been allowed by the U.S. Patent Office and is expected to issue in April or May 2009, we cannot assure that our present patents or any which may be issued to us in the future will be upheld if challenged in court or that we will be able to obtain additional patents. We cannot assure that our patents, if issued, can be enforced against infringers. We also cannot assure that our products will not infringe patents owned by others, licenses to which may not be available to us. Our inability to obtain and maintain our patents, avoid infringement of our products by others or to obtain licenses to any necessary patents could have a materially adverse effect on our financial condition, results of operations and our ability to remain in business (See "Patents And Patent Applications" under "BUSINESS").

# 27. We Do Not Anticipate Paying Any Dividends

We have not paid any dividends in the past and do not anticipate paying any dividends in the foreseeable future. This may depress the price of our Shares, as a non-divided paying stock may not appeal to certain investors (See "Dividends" under "BUSINESS").

# 28. Lack of Control by Investors

The Company's directors have virtually unlimited latitude in making business decisions for the Company. Since the Company's Articles of Incorporation do not provide for cumulative voting in the election of directors, the investors in this Offering, even if all of the Shares being offered are sold and the investors were to vote as a group, they will not be able to elect any of the directors of the Company or exert any influence on the Company's management, operations or policies (See "DESCRIPTION OF SECURITIES").

## 29. Broad Indemnification of Officers and Directors

Our By-Laws provide that we will indemnify our directors and officers to the fullest extent permitted by law, even if this indemnification is against acts for which insurance may not be available to us.

#### 30. Unaudited Financial Statements

The Financial Statements included in this Offering Circular were prepared internally by our management and have not been reviewed or audited by an independent accounting party. While these Financial Statements, in the opinion of the management of the Company, contain all adjustments of a normally recurring nature necessary for a fair statement of the Company's financial condition and its results of operations for the dates and periods indicated, we cannot assure that our Financial Statements would meet the standards of or satisfy an independent accounting party (See 'MANAGEMENT'S DISCUSSION AND ANALYSIS" and "FINANCIAL STATEMENTS").

#### 31. New Accounting Rules or Standards

The Financial Accounting Standards Board ("FASB"), the SEC or other rulemaking authorities may issue new accounting rules or standards in the future which may adversely affect our business and the cost of preparing our financial statements, SEC filings and reports to our shareholders (See "MANAGEMENT'S DISCUSSION AND ANALYSIS" and "FINANCIAL STATEMENTS").

#### FORWARD-LOOKING STATEMENTS

Some of the statements under "Risk Factors" and elsewhere in this Offering Circular are forward-looking statements that involve risks and uncertainties. These forward-looking statements include statements about our plans, objectives, expectations, intentions and assumptions, and other statements contained in this Offering Circular may not be statements of historical fact. You can identify these statements by words such as "may," "will," "should," "could," "estimates," "plans," "expects," "believes," "intends" and similar expressions. We cannot guarantee future financial results, levels of activity, performance or achievements. Our actual results and the timing of certain events may differ significantly from those discussed in the forward-looking statements. Factors that might cause such a discrepancy include those discussed in "RISK FACTORS" and elsewhere in this Offering Circular. You are cautioned not to place undue reliance on any forward-looking statements contained in this Offering Circular.

#### **CAPITALIZATION**

The following table sets forth the capitalization of the Company on December 31, 2008, on a fully diluted basis and as adjusted to reflect the sale by the Company of all of the 5,000,000 Shares presently being offered, assuming exercise of all of the presently exercisable Stock Options and outstanding Warrants and conversion of all of the presently outstanding Convertible Notes and accrued interest to maturity.

Actual Adjusted

Number of \$0.01 par value Shares authorized, 40,000,000;
7,427,060 Shares presently outstanding; 11,166,960
Shares outstanding on a fully-diluted basis, prior to the
Offering, including in the fully-diluted number of Shares
Outstanding, the issuance of:

\$ 74,271

(a) 603,000 Shares from the exercise of exercisable
Stock Options at a average price of \$2.48 per share \$1,495,400 \$ 1,495,400

111,670

Shareholders' equity (deficit)

(b) 536,900 Shares from the exercise of Warrants at a price of \$3.75 per share	\$2,013,375	\$ 2,013,375
(c) 2,600,000 Shares from the conversion of \$1,000,000 of 6% Convertible Notes* and accrued interest to maturity at \$0.50 per share	\$1,300,000	\$ 1,300,000
Additional Paid-In Capital	\$8,521,292	\$13,521,292
Retained earnings (deficit)	(\$9,523,383)	(\$ 9,523,383)
Current Net Income (Loss)	(\$ 189,391)	(\$ 189,391)
Total Shareholders' Equity	(\$1,136,192)	\$ 3,263,808

We are not in default or in breach of any note, loan, lease, indebtedness or financing obligation.

#### DILUTION

The 7,427,060 Shares presently outstanding were acquired by our present shareholders at an average cost of \$1.15 per share. This average cost per share will be reduced to an average cost of \$0.90 per share, if all of the \$1,000,000 of Convertible Notes presently outstanding are converted, including accrued interest to maturity, into Shares, which we cannot assure. Any exercise of Stock Options at an average exercise price of \$2.48 per share or exercise of Warrants at \$3.75 per share would not be economically dilutive to the purchasers of Shares in this Offering.

However, the difference between the price of the Shares being offered and the Company's present net tangible book value per Share after the Offering constitutes substantial economic dilution to the new investors in this Offering. Net tangible book value per Share is determined by dividing the Company's tangible book value (total tangible assets less total liabilities) by the number of outstanding Shares.

At December 31, 2008, the Company's net tangible book value was (\$1,136,192) or (\$0.15) per Share. After giving effect to the net proceeds from the sale of all of the 5,000,000 Shares being offered to the public at a price of \$1.00 per Share, the Company's pro forma net tangible book value would be \$3,263,808 or \$.026 per Share. This represents an immediate decrease of \$0.74 per Share to the purchasers of Shares in this Offering, and an increase in the net tangible book value of \$0.41 per Share at no cost to our existing shareholders. This presents a risk which must be carefully evaluated by prospective purchasers of the Shares being offered.

Our Chairman and CEO, our other executive officers and our directors have been issued or purchased Shares and/or were granted conversion rights to acquire Shares at significantly lower prices than the price at which the 5,000,000 Shares are presently being offered (See "CAPITALIZATION," "TRANSACTIONS WITH MANAGEMENT" and "DESCRIPTION OF SECURITIES").

#### **USE OF PROCEEDS**

If all of the 5,000,000 Shares being offered are sold, the estimated net proceeds of \$4,400,000, after Commissions of \$500,000 and offering expenses of \$100,000, are expected to be used as follows:

(a) \$2,500,000 of the net proceeds will be used to purchase components, assemble ECP Systems, purchase CPD and SDD Systems, recruit and train nurses and technicians to

<sup>\*</sup> The Notes are secured by all of the assets of the Company and have preference over the Common Stock in the event of the liquidation or dissolution of the Company (See "DESCRIPTION OF SECURITIES").

operate the Systems, and pay overhead and sales costs to sell or rent the Systems for per hour or per test rental charges to physicians, group practices, clinics and hospitals;

- (b) \$500,000 of the net proceeds will be used in 2009 and 2010 to pay the initial costs of two randomized, controlled clinical studies of (a) our ECP and CPD Systems in the treatment of Stable (chronic) Heart Failure and Angina and (b) our ECP System in the treatment of Acute Heart Failure for submission to Medicare, provided at least \$2.5 million of Shares is sold;
- (c) \$300,000 of the net proceeds will be used to employ a sales manager for the North American Market and a sales manager for Foreign Markets.
- (d) \$100,000 of the net proceeds will be used in 2009 and early 2010 to test market a mailing program to seniors in retirement communities extended care facilities and nursing homes to attract seniors to pay for the use of our ECP System to treat less severe Angina and Heart Failure, until Medicare coverage for less severe Angina and chronic Heart Failure is obtained.
- (e) The \$1,000,000 balance of the net proceeds will be used for general corporate purposes, including paying up to \$200,000 of the Company's payables and accrued expenses. To the extent the remaining funds are not needed for general corporate purposes, they may be used to expand the activities described above.

If less than all of the Shares being offered are sold, the amounts allocated for the above applications may be proportionately reduced or the applications may be delayed or eliminated.

If only 50% of the Shares being offered are sold, we believe the net proceeds of such sales will be sufficient to fund our operations for at least the next twelve (12) months.

None of the net proceeds of this Offering will be used to retire the outstanding Convertible Notes or pay for any services or property provided to us in the past by any of our officers, directors, employees or stockholders.

If the Company's financial resources and revenues in 2009 and 2010 are not sufficient, after paying its costs of operations, to continue to fund the remaining \$500,000 of the estimated cost of the clinical studies referred to in subparagraph (b) above, the clinical studies may have to be abandoned and the \$500,000 to be spent on these studies in 2009 and 2010 may be lost.

# THE OFFERING & PLAN OF DISTRIBUTION

We are presently offering 5,000,000 of our Shares to the public at a price of \$1.00 per Share on a "best efforts" basis. We can give no assurance that any or all of the Shares being offered will be sold. The offering price of the Shares was arbitrarily determined and is not based on any established criteria of value. Investors in our Shares will not have the benefit of an underwriter's assessment of the merits of the Company or the Offering. No pre or post-offering market capitalization of our Company can be determined until we have operated profitably for a full year, which we cannot assure will occur.

There will be no escrow of the funds from the purchasers of the Shares, and there is no minimum number of Shares that must be sold to complete or close this Offering. As a result, the proceeds of the sales of Shares will be immediately available for use by the Company. We cannot assure that the proceeds of this Offering will be sufficient to carry out our current business objectives or meet our future needs.

Within 60 days after the closing date of the Offering, the Company will issue at no cost to the purchasers of Shares in this Offering, one-half Class A Warrant for each Share purchased and one-half Class B Warrant for each Share purchased in the Offering. Two (2) Class A Warrants may be exercised to purchase one (1) Share at a price of \$1.50 at any time during a period of six (6) months, commencing twelve

(12) months from the closing date of this Offering. Two (2) Class B Warrants may be exercised to purchase one (1) Share at a price of \$2.00 at any time during a period of twelve (12) months, commencing twelve (12) months from the closing date of this Offering. The Warrants contain no anti-dilution provisions. The Class A and B Warrants may be redeemed by the Company during their respective exercise periods by thirty (30) days prior written notice to the holders if the market price of the Shares is at least 50% higher than their respective exercise prices for a period of five (5) trading days.

The Class A and B Warrants and the Shares issuable upon exercise of the Class A and B Warrants are not being registered in the Registration Statement of which this Offering Circular is a part. As a result, no market for the Class A or B Warrants is expected to arise. Shares purchased by the exercise of the Class A and B Warrants, if any, may be sold publicly pursuant to Rule 144 of the Securities and Exchange Commission after six (6) months by holders who are not officers, directors or five percent (5%) owners of the Company's Shares. Officers, directors and 5% owners of the Company's Shares may sell Shares purchased by the exercise of the Class A or B Warrants, if any, publicly pursuant to Rule 144 after six (6) months, subject to certain volume limitations.

We presently have no agreements with any Broker/Dealers to sell any of the Shares being offered. Broker/Dealers who enter into a Selling Dealer Agreement with us, if any, will receive a commission of up to ten percent (10%) of the gross proceeds from the sale of Shares by them, if any. We will also issue to such Broker/Dealers warrants, exercisable to purchase Shares at a price of \$1.10 per Share (10% higher than the price per Share to investors in this Offering) for a period of two (2) years, commencing one (1) year following the closing date of this Offering, in an amount up to ten percent (10%) of the number of Shares sold by them in this Offering, if any. The warrants issuable to such Broker/Dealers and the Shares underlying such warrants, if any, are not included in the Registration Statement of which this Offering Circular is a part, and any Shares purchased by the exercise of such warrants, if any, may be sold publicly after six (6) months pursuant to Rule 144 of the Securities and Exchange Commission, unless the purchaser acquires Shares in an amount equal to or greater than 5% of the then outstanding Shares, in which event such Shares may be sold publicly pursuant to Rule 144 after six (6) months, subject to certain volume limitations.

While the compensation of Broker/Dealers who enter into Selling Dealer Agreements with us, if any, has not been cleared with or approved by the National Association of Securities Dealers ("NASD"), we believe the compensation is within the NASD's rules on compensation of Broker/Dealers participating in an offering such as this Offering. While we have not entered into any agreements to do so, we may employ consultants to advise us on financial matters in connection with this Offering.

This Offering of Shares will terminate on the earlier to occur of the sale of all of the 5,000,000 Shares being offered or one hundred eighty (180) days following the qualification date of this Offering Circular, unless the offering is extended without notice by the Company for an additional one hundred twenty (120) days.

# THE COMPANY

#### General

Cardiomedics, Inc. ("we", "our" or "us" or the "Company") is presently engaged in developing, manufacturing, distributing, marketing, selling, renting and operating of (a) External Counter Pulsation or "ECP" Systems to treat Angina and Angina patients who also suffer from Heart Failure, (b) Cardio Pulmonary Diagnostic or "CPD" Systems to assess the cardiopulmonary condition of Heart Failure patients and (c) Sleep Disorder Diagnostic or "SDD" Systems to diagnose and evaluate therapies for the treatment of sleep disorders which, if not treated, can worsen cardiac conditions. All of our products are used to treat patients in physicians' or group practice's offices, clinics or the outpatient departments of hospitals on an outpatient basis. We also plan to acquire and distribute other medical devices complimentary to our present products that can be sold or rented to the same kinds of parties to whom we market our present products.

Our ECP Systems have been cleared for sale in the United States by the FDA for the treatment of Angina, Heart Failure, Heart Attacks and Cardiogenic Shock, but are currently covered (reimbursed) by Medicare and most insurance companies and HMOs only for the treatment of severe, Class III or IV Angina patients who are not amenable to balloon angioplasty or bypass surgery and such Angina patients who also suffer from Heart Failure. About 30% to 40% of Angina patients also suffer from Heart Failure. This limits the market for our ECP Systems to an estimated 150,000 of the 6 million persons who suffer from Angina in the United States.

We plan to commence two randomized, controlled clinical trials of our ECP System in 2009-2010, one in the treatment of Stable (chronic) Heart Failure and Angina and one in the treatment of Acute Heart Failure, in order to obtain coverage for our ECP System in the treatment of less severe Angina and Stable Heart Failure and in the treatment of Acute Heart Failure. About 4 million people in the United States suffer from Stable Heart Failure, about 400,000 Americans die from Heart Failure each year, and there are about 1 million hospitalizations for Acute Heart Failure each year in the United States. The treatment of Heart Failure is the largest single cost to Medicare at about \$40 billion per year. About 6 million people in the United States suffer from Angina, which is a large cause of emergency room visits and hospitalizations at significant cost to Medicare. Later, we plan to conduct a new clinical trial of our ECP System in the treatment of Heart Attacks, which kill about 500,000 Americans each year and is one of Medicare's largest costs. (See "Medicare Reimbursement" under "BUSINESS").

Our ECP Systems are the only such devices which have been shown in clinical studies, published in peer-reviewed medical journals, to significantly reduce (a) mortality and the incidence of hospitalizations in the treatment of Stable Heart Failure, (b) the incidence of Angina attacks, nitroglycerine use (a vasodilator used to ease the pain of such attacks) and hospitalizations in the treatment of Angina, and (c) mortality in the treatment of Heart Attacks and Cardiogenic Shock (See "Results of Clinical Studies" under "BUSINESS").

U.S. Patent No. 7,244,225 was issued to us on July 17, 2007, covering our new, Graduated™ Low Pressure ECP Regimen to treat Stable Heart Failure and other medical conditions and certain improvements in our ECP System. Another U.S. Patent, covering an advanced, Graduated™ Low Pressure ECP Regimen to treat Stable Heart Failure, has been allowed by the U.S. Patent Office and is expected to issue in April or May 2009. This Graduated™ Low Pressure ECP Regimen enabled our ECP System to significantly reduce mortality and the incidence of hospitalizations in the treatment of Heart Failure and Angina patients with Heart Failure (See "Results of Clinical Studies" under "BUSINESS").

Our CPD and SDD Systems have been cleared for sale in the United States by the FDA and their use is covered and reimbursed by Medicare and most insurance companies and HMOs. All of our present products are CE Marked and eligible for sale in the European Union, and our manufacturing facility is ISO Certified.

Physicians and group practices in the U.S. and foreign countries are not accustomed to spending up to \$30,000, \$100,000 or \$120,000 for equipment to be used in their offices. Clinics and hospitals also resist buying "big ticket" equipment, as they have limited capital equipment budgets and credit lines. Although we will continue to sell our ECP Systems for up to \$60,000 to distributors and up to \$100,000 to customers, our CPD Systems for up to \$20,000 to distributors and up to \$30,000 to customers and our 3 Bed SDD Systems for up to \$90,000 to distributors and up to \$120,000 to customers, to avoid the reluctance of physicians, group practices, clinics and hospitals to buy "big-ticket" equipment or lease it under long-term, non-cancellable leases, we plan to devote our principal efforts in the future to renting our products for a per hour of per test charge to physicians, group practices, clinics and hospitals under Rental Agreements, which can be cancelled by the renter on two or three months prior written notice (See "Per Hour and Per Test Rental Programs" under "BUSINESS").

Under the Rental Agreements, we will provide, at our expense, the product to the renter and, in some instances, a nurse or technician to operate it, on a "turn key" basis with no up-front cost to the physicians, group practices, clinics or hospitals for a period of five (5) years or longer, subject to earlier termination, as described above. We also provide, at our cost, parts to replace defective parts of our products and preventative maintenance services throughout the terms of the Rental Agreements. A nurse or technician is

expected to be able to operate a 3 Bed SDD System. If we provide an operator, the renter will pay us a fixed per hour or per test rental charge, which is based upon about half of what Medicare pays for the therapy or test, even though insurance companies, HMOs and private pay patients may pay more or less than Medicare. If we do not provide an operator, the per hour or per test charge will reflect the absence of this cost.

Since we will be providing our Systems and, in some instances, the services of a nurse or technician, at our expense, our Rental Agreements will require the renter to pay for a minimum number of hours or tests per month. In the United States, if we provide the operator, these minimums are expected to be up to \$5,600 per month for ECP Systems, up to \$2,400 per month for CPD Systems or up to \$10,000 per month for 3 bed SDD Systems, which we believe will cover the cost of one nurse or technician to operate up to two ECP Systems and one CPD System and one sleep technician to operate a 3 bed SDD System. These minimums are expected to enable us to recover the cost of the applicable System in about 10-12 months, but we cannot assure this will be possible. If we rent these Systems without operators, the per test or per hour charges and minimum monthly rental will reflect the absence of this cost.

To make our Rental Agreements with substantial monthly minimum charges acceptable to physicians, group practices, clinics and hospitals, our Rental Agreements may be cancelled by the renter on two (2) or three (3) months prior written notice and returning the System to us. We plan to rent our Systems to parties who have sufficient patient volume to make providing the Systems and operators profitable to us. We cannot assure that we will be able to do so or that we can successfully sell or rent a sufficient number of any Systems which may be returned to us to other physicians, group practices, clinics or hospitals (See "Per Hour and Per Test Rental Program" under "BUSINESS").

We are investigating the potential of our marketing or distributing other cardiovascular and cardiopulmonary devices, which we might also rent, sell or lease to physicians, group practices, clinics and hospitals. We cannot assure that we will be able to successfully consummate any agreements to do so.

We were incorporated under the laws of the State of Nevada on August 25, 1986. Our office and factory is located at 18872 Bardeen Avenue, Irvine, CA 92612. Our telephone number is 1-949-863-2500, our toll free telephone number is 1-888-849-0200, and our President, John McCallum, can be contacted at 1-949-863-2500, Extension 106.

#### **Holders of Common Stock**

As of December 31, 2008, we had approximately 185 holders of record of our Shares.

#### Dividends

We have never paid cash dividends on our Shares and do not anticipate paying cash dividends in the foreseeable future. Any future determination as to the payment of cash dividends will be dependent upon our financial condition, the results of operations and other factors then deemed relevant by our Board of Directors.

# **Shares Authorized For Issuance Under Equity Compensation Plans**

The following table provides information as of December 31, 2008 with respect to Shares that may be issued through our employee compensation plans (stock option plans):

NUMBER OF SHARES TO BE ISSUED UPON EXERCISE OF OUTSTANDING

WEIGHTED-AVERAGE EXERCISE PRICE OF OUTSTANDING NUMBER OF SHARES AVAILABLE FOR FUTURE ISSUANCE UNDER EQUITY COMPENSATION PLANS (EXCLUDING SHARES IN

	OPTIONS	OPTIONS	COLUMN (a))
Plan Category	(a)	(b)	(c)
Equity Compensation Plans approved by security holders	1,088,000	\$2.48	1,112,000
Equity Compensation Plans not approved by security holders	None	None	None
Total	1,088,000	\$2.48	1,112,000

## MANAGEMENT'S DISCUSSION AND ANALYSIS

# **CRITICAL ACCOUNTING POLICIES**

#### **Unaudited Financial Statements**

The Financial Statements appearing in this Offering Circular were prepared internally by our management and have not been reviewed by, passed-upon or audited by any independent accounting firm or person. However, in our opinion, these Financial Statements contain all adjustments of a normally occurring nature necessary for a fair statement of the Company's financial condition as of the date specified and its results of operations for the periods shown.

# **Revenue Recognition**

Our revenue presently includes revenues from the sale of ECP Systems, the repair of ECP Systems and the sale of CPD Systems, as well as the sale of extended service contracts for our ECP Systems. Our future revenues are expected to consist mainly of rental charges from the rental and operation of our ECP, CPD and SDD Systems.

In accordance with Staff Accounting Bulletin 104, "Revenue Recognition", we recognize revenue from products sold once all of the following criteria for revenue recognition have been met: (i) persuasive evidence that an arrangement exists, (ii) the products have been shipped, (iii) the prices are fixed and determinable and not subject to refund or adjustment and (iv) collection of the amounts due is reasonably assured.

Revenues from the sale of our products are recognized upon shipment and passage of title of the products to the customer, provided that all other revenue recognition criteria have been met, Generally, on sales of our products, customers are required to insure the goods from our place of business. Accordingly, the risk of loss transfers to the customer once the goods have been shipped from our warehouse. We sell our products primarily through commission sales representatives in the United States. We appoint distributors to sell our products outside the United States, and we recognize revenue upon shipment, provided that all other revenue recognition criteria have been met, and ownership risk has transferred. In some cases, particularly on sales through group purchasing organizations, we may have post shipment obligations such as installation and/or in acceptance provisions. All of our products are sold with a one year warranty, which includes parts and labor to replace defective parts. In the case of foreign sales of our products, we provide only a one-year parts replacement warranty, and the distributor provides the labor. We offer extended service contracts with a one-year or multi-year term. On extended service contracts with a multi-year term, revenue exceeding the amount applicable to future years is deferred and is ratably recognized in each subsequent year.

Revenues from the rental of our products under Rental Agreements for per hour or per test fees are recognized when due from customers in the United States and when received from customers outside the United States. Under our Rental Agreements in the United States, we presently pay our independent sales representatives a fixed percentage of the revenues for their services in securing the Rental Agreements throughout the usual five (5) year term of the Rental Agreements, and we provide parts to replace defective parts of the products, labor to install the parts and labor to adjust and maintain the products throughout the usual five (5) year term of our Rental Agreements. Under our Rental Agreements outside the United States, we provide parts to replace defective parts of the products during the usual five (5) year terms of the Rental Agreements, and our distributor provides labor to install the parts and labor to adjust and maintain the products during the usual five (5) year term of our Rental Agreements. We pay the distributors a fixed percentage of the revenues we receive from the rental of our products outside the United States for their services in securing the Rental Agreements throughout the usual five (5) year terms of the Rental Agreements, and a fixed percentage of the revenues we receive for the distributor's providing labor to install parts to replace defective parts of the products and labor to adjust and maintain the products during the usual five (5) year term of the Rental Agreements.

Allowances for doubtful accounts are based on estimates of losses on customer receivable balances, based on historical losses, adjusted for current economic conditions and specific customer experience. This requires the use of judgment and assumptions, which cannot be assured. Changes in economic conditions could have a material effect on balances reserved for doubtful accounts. Our credit losses in 2008 and 2007 were 2% and 0% of revenues, respectively.

#### Inventories

Inventories consist of raw materials and component parts, work in process and finished good products and accessories. Inventories are recorded at the lower of cost or market, cost being determined principally by use of the average-cost method, which approximates the first-in, first-out method. Cost is determined at the actual cost for raw materials, and at production cost (materials, labor and indirect manufacturing overhead) for work-in-process and finished goods.

Products provided to physicians or hospitals for sales evaluation, demonstration purposes or medical training are included in inventory, provided the products are ultimately intended to be sold. These units are written down to reflect their net realizable values.

We write-down our inventory for estimated obsolescence equal to the net realizable value of the obsolete inventory. Product obsolescence may be caused by changes in technology, discontinuance of a product line, replacement products in the marketplace or other competitive situations. We maintain a reserve on inventories of products that we consider to be slow moving or obsolete, to reduce the inventory to its net estimated realizable value. Once specific inventory is written-down, the write-down is permanent until the inventory is physically disposed-of.

#### Goodwill

We have adopted the provisions of Statement of Financial Accounting Standards "SFAS" No. 142, "Goodwill and other Intangible Assets." As a result of our adoption of SFAS No. 142, our goodwill is no longer amortized, but is subject to an annual impairment test, or whenever events or changes in circumstances indicate that the carrying value may not be recoverable. There was no goodwill or impairment loss recognized on goodwill during the fiscal years ended December 31, 2008 and 2007.

## Impairment of Long-Lived Assets

SFAS No. 144, "Accounting for Impairment or Disposal of Long-Lived Assets" requires that long-lived assets, such as property and equipment and purchased intangibles subject to amortization, be revised for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset may

not be recoverable. Recoverability of the asset is measured by comparison of its carrying amount to the undiscounted future cash flows the asset is expected to generate. If such assets are considered to be impaired, the impairment to be recognized is measured as the amount by which the carrying amount of the asset exceeds its fair market value.

Estimates of expected cash flows represent management's best estimate, based on currently available information and reasonable and supportable assumptions. Any impairment recognized in accordance with SFAS No. 144 is permanent and may not be restored. To date, we have not recognized any impairment of long-lived assets in connection with SFAS No. 144.

#### **Deferred Taxes**

We record a valuation allowance to reduce any deferred tax assets to the amount that is more likely than not to be required. The company has considered estimated future taxable income and ongoing tax planning strategies in assessing the amount needed for the valuation allowance based on these estimates. We have no deferred tax assets.

#### **Stock-based Compensation**

We have not accounted for our employee stock-based compensation plans under the recognition and measurement principles of Accounting Principles Board Opinion No. 25, "Accounting for Stock issued to Employees" and related interpretations. We plan to adopt the disclosure provisions of SFAS No. 144, "Accounting for Stock-Based Compensation," as amended by SFAS No. 148. "Accounting for Stock-Based Compensation – Transition and Disclosure," when required by law or regulation.

# **Forward-Looking Statements**

The statements contained herein that are not historical facts may consist of forward-looking statements that involve a number of known and unknown risks and uncertainties that could cause our actual results to differ materially from those discussed or anticipated in such forward-looking statements.

Potential risks and uncertainties include, among other factors, general business conditions, government regulations pertaining to medical device approvals and manufacturing practices, competitive market conditions, success of our business and rental strategies, delays in receipts of orders, changes in the mix of products sold, availability of suppliers, concentration or sales in certain markets and to certain customers, changes in manufacturing efficiencies, development and introduction of new products, fluctuations in margins, timing of significant orders, and other risks and uncertainties currently unknown to management.

#### **Results of Operations**

The following table sets forth certain items in the our unaudited statements of income as a percentage of net revenues for the years ended December 31, 2008 and 2007.

	Years Ended December 31 (Unaudited)		
·	<u>2008</u>	2007	
Net Revenues	100.0%	100.0%	
Cost of Goods	36.0	42.0	
Gross Profit	63.9	58.0	
SG&A & Regulatory	84.3	97.7	
R&D & Clinical Trials	2.4	0.0	
Interest expense & Depr	4.3	5.9	
Income taxes	0.06	0.1	

#### **Net Revenues**

Net Revenues increased by 33% to \$1,142,289 in 2008, from \$860,282 in 2007, due to an increase in the number of products sold.

## **Cost of Goods, Gross Profit and Cost of Sales**

Cost of Goods was 36.1% of Net Revenues in 2008, compared to 42.0% of Net Revenues in 2007, due to lower component and manufacturing costs in 2008. Gross Profit was 63.9% of Net Revenues in 2008, versus 58.0% of Net Revenues in 2007, due to higher revenues in 2008.

#### Selling, General and Administrative Expenses

Selling, General and Administrative or "SG&A" expenses were 83.9% of Net Revenues in 2008, versus 98.9% of Net Revenues in 2007. In 2007, we terminated our direct, salaried sales force, reduced to two Regional Sales Managers and, in late 2007 and early 2008, we eliminated our two remaining Regional Sales Managers and began appointing distributors to sell our products outside the United States and independent sales representatives on a straight commission basis to sell our products in the United States.

#### Research And Development (R&D) and Clinical Trials

R&D and clinical trial expense was 2.8% of Net Revenues in 2008, compared to 0% of Net Revenues in 2007, due to our commencing the development of a new, advanced ECP System in 2008.

## **Net Profit (Loss)**

As a result of lower SG&A expenses in 2008 and manufacturing costs as a percentage of revenues and the benefit of a prior year accounts payable adjustment of \$120,047, we had a Net Loss of \$189,371 or \$0.03 per Share in 2008, based on 7,427,980 Shares outstanding, compared to a Net Loss of \$393,060 or \$0.05 per Share in 2007, based on 7,187,060 Shares then outstanding.

#### Cash flows

Net Cash consumed by operating activities was \$289,321 in 2008, compared to \$173,836 in 2007.

#### **Liquidity and Capital Resources**

We had working capital of \$20,456, at December 31, 2008, compared to (\$357,271) at December 31, 2007. Cash increased by \$110,679 to \$117,105 at the end of 2008, from \$6,426 at the end of 2007.

If only half of the Shares being offered are sold, we believe the net proceeds will be sufficient to meet our operating needs for at least the next twelve months.

We have outstanding 6% Senior, secured, convertible notes ("Notes") to our chief executive officer in the amount of \$900,000 and Notes to two directors in the amount of \$50,000 each. These Notes bear interest at 6% per annum, mature at various dates, from 2010 to 2013 and are convertible, with accrued interest, into Shares at a price of \$0.50 per share.

At December 31, 2008, we had a net loss carry-forward of \$7,301,805, which will reduce any federal income tax expense we may incur in future years to this extent.

#### **BUSINESS**

#### General

In 2007 we eliminated our direct sales force, which was unable to sell a sufficient number of units to our products to offset our manufacturing, marketing and sales costs. In late 2007 and early 2008, we eliminated our two Regional Sales Managers, and we began appointing independent sales representatives ("Sales Reps") to sell our products on a straight commission basis in the U.S. and distributors to sell our products in foreign countries. In 2008, our revenues increased and our loss decreased, compared to 2007 (See "FINANCIAL STATEMENTS").

#### **Results of Clinical Studies**

Our ECP Systems are the only ECP devices that have been shown in clinical studies, published in peer-reviewed medical journals, to produce the following clinical benefits:

- (a) Reduce the incidence of Angina attacks in 58 Canadian Cardiology Society Functional ("CCSF") Class II-IV Angina patients by 76%, reduce nitroglycerine use (a vasodilator used to ease chest pain from the lack of blood flow to the heart due to blockages in one or more of the coronary arteries) by 77% and reduce the incidence of hospitalizations for Angina by 90% in the year following 35 hours of ECP therapy (one hour per day, five days a week for seven weeks), compared to the year prior to the ECP therapy<sup>(1)</sup>. Emergency room visits and hospitalizations for Angina is a major cost to Medicare;
- (b) Reduce mortality in 59 New York Heart Association ("NYHA") Class II-IV Stable (chronic) Heart Failure patients to 1.85% in the year following 35 hours of ECP therapy under our patented, Graduated Low Pressure ECP Regimen<sup>(2)</sup>, a 90% reduction from the American Heart Association's published figure of 19.1% annual mortality from Stable Heart Failure<sup>(3)</sup>, a savings of 17 lives per hundred ECP treated patients, and reduce the incidence of hospitalization by 87.5% in the year following 35 hours of ECP, compared to the prior year<sup>(2)</sup>. The cost of treating Stable and Acute Heart Failure is the largest single cost to Medicare and is estimated at about \$40 billion annually;
- (c) Reduce mortality during the hospital stay to 6.5% in 108 Killip Class II Heart Attack patients (the most common type of Heart Attack), who received 4 hours of ECP within 24 hours of the onset of the Heart Attack Symptoms, a 56% reduction from mortality of 14.7% in the 116 Heart Attack patients in the Control Group, who received only conventional medical therapy<sup>(4)</sup>, a savings of 8 lives per hundred ECP treated patients; and
- (d) Increase survival of 20 patients in Cardiogenic Shock to 35% in the month following the ECP treatment, an increase of 233%, from the published survival figure of 15% from this condition<sup>(5)</sup>, a savings of 20 lives per hundred ECP treated patients.

<sup>(1)</sup> Weisfogel G et al, External Counterpulsation Produces a Significant Reduction in Stable Angina Class, Episodes, Medication Use, and Hospitalization. Am J. Cardiol, 1980;45:349-356.

<sup>(2)</sup> Vijaraghavan K et al, New Graduated Pressure Regimen for External Counterpulsation Reduces Mortality and Improves Outcomes in Congestive Heart Failure: A Report From the Cardiomedics External Counterpulsation Patent Registry. CHF, 2005; 11:147-152.

<sup>(3) 2007</sup> Heart Failure and Stroke Statistical Update, American Heart Association, Dallas, Tx.

<sup>(4)</sup> Amsterdam E et al, Clinical Assessment of External Pressure Circulatory Assistance in Acute Myocardial Infarction. Am Heart J, 1980;45:349-456.

<sup>(5)</sup> Soroff HS et al, External Counterpulsation: Management of Cardiogenic Shock After Myocardial Infarction. JAMA, 1974; Vol229; 11:1441-1450.

## **New ECP System**

We are developing a new ECP System, which will be smaller, lighter in weight to reduce shipping cost and is expected to cost less to manufacture than our present ECP System. It will also be more quiet, which is important in busy medical offices and very important in hospitals. It will function the same as our present ECP System, so we do not believe any clearance from the FDA to market the new ECP System will be required.

The mechanical portion of the development of the new ECP System has been completed and we have a working prototype. The software design and validation is expected to be completed in late May 2009, at which time field testing for one month will commence. Barring any unforeseen problems, we expect the new ECP System should be available for sale by the end of June 2009.

We ceased manufacturing our present ECP System in March 2009, when we used-up all of our available components. To avoid having an inventory of our present ECP Systems or components, which we would have to mark down in price or write-off when the new ECP System is available for sale, we have not ordered components to build more of our present ECP Systems, due to the long lead-times. Also, one component of the software of our present ECP System is no longer available from the supplier, and there is no assurance it could be successfully duplicated. As a result, we expect to have none of our present ECP Systems to sell until the end of June 2009 and, perhaps, later, which could adversely affect our revenues and financial results in the quarter ended June 30, 2009 and, possibly, the quarter ended September 30, 2009.

However, the lower cost to manufacture and attractive small size and quiet operation of the new ECP System is expected to make any cost of the change-over to the new ECP System economically positive.

We also plan to expand the software capabilities of the new ECP System and, in late 2009, we expect to begin marketing an advanced ECP System with new software capabilities under our recently issued U.S. Patent No. 7,244,225, among which will be the on-board computer of the ECP System being able to automatically adjust the advanced ECP System to produce and maintain throughout the one-hour ECP therapy period whatever pressures are selected by the physician to treat the patient's condition.

Since 35 one-hour ECP treatments are typically administered over a period of seven weeks, the computer will also remember the patient (by his I.D. number) and the settings and will produce and maintain the same pressures in subsequent one-hour ECP therapy sessions, compensating for any variations in the patient's blood pressure, heart rate and ECG during the therapy and reducing the potential for errors by nurses or technicians.

The design of the advanced ECP System, its new software and its new Operation Manual must be submitted to the FDA in a 510(k) Notification, and the advanced ECP System must be cleared for sale by the FDA before it can be sold in the United States or exported. This process is expected to take until late 2009, but we cannot assure that FDA clearance will be received by late 2009, when we hope to introduce the advanced ECP System, or at all. If the advanced ECP System is delayed, we will continue to rent and sell the new ECP System, as the only physical difference between these ECP Systems, is in its software/circuit boards and display screen capabilities.

#### **Recent Patent Issuance**

In July 2007, U.S. Patent No. 7,244,225, covering our Graduated<sup>™</sup> Low Pressure ECP Regimen to treat Stable Heart Failure and other conditions and certain improvements to our ECP System, was issued to us by the U.S. Patent and Trademark Office. This Graduated<sup>™</sup> Low Pressure ECP Regimen enabled us to achieve the results in Stable Heart Failure described above. Another U.S. Patent, covering an advanced, Graduated<sup>™</sup>

## **Medicare Reimbursement for ECP Therapy**

Medicare currently pays an average of \$165 nationally for each hour of ECP therapy for the treatment of severe, Class III-IV Stable Angina patients, who are not amenable to balloon angioplasty or bypass surgery, an average of \$5,775 for 35 hours of ECP therapy. About 40% of severe Angina patients also suffer from Heart Failure. Medicare will pay for additional hours of ECP, if it is shown by an appropriate diagnostic test to be medically necessary for Angina patients who meet the criteria for coverage. ECP therapy is administered by a trained nurse or technician.

In mid-2005, we applied to Medicare for coverage of ECP for the treatment of CCSF Class II (mild) Angina, we asked for removal of the "not amenable to balloon angioplasty or bypass surgery" limitation on coverage of ECP for CCSF Class III or IV (severe) Angina patients, we requested coverage of ECP for treatment of NYHA Class II-IV Heart Failure and we requested coverage of ECP for the treatment of Killip Class II-IV Heart Attacks and the treatment of Cardiogenic Shock, the most serious complication of a Heart Attack.

In March 2006, Medicare denied our application for all of the additional coverages we requested for ECP. Medicare expressed a concern that our clinical study of ECP in the treatment of Heart Failure did not include a control group, although Medicare's published coverage rules do not require a clinical study with a control group. In our clinical study, we treated three groups of Heart Failure patients at different levels of pressure applied under our Graduated™ Low Pressure ECP Regimen, at "high," "medium" or "low" pressure.

The Heart Failure patients in the low pressure group in our Heart Failure Study had a mortality rate of only 1.85%, (a 90% reduction from the American Heart Association's published figure of 19.1% mortality from Heart Failure in the United States), a savings of 17 lives per 100 patients treated, and a reduction in the incidence of hospitalizations of 87.5% in the year following 35 hours of our ECP therapy, compared to the year following the ECP therapy. The patients in the mid-pressure group had a mortality rate of 7.69% and a reduction in hospitalizations of 82.6%. The patients in the high pressure group had a mortality rate of 8.82% and a reduction in hospitalizations of only 57.1%, demonstrating a clear trend of improvement at lower pressures. However, our study did not include a control group that received only conventional medical therapy.

Medicare also expressed concern that our Heart Attack Study (which had a control group) and our Cardiogenic Shock Study (which did not have a control group) were both performed a number of years ago, although mortality from both of these conditions has not changed significantly since these Studies were conducted.

While Medicare did not grant the expanded coverages for ECP that we requested, Medicare increased the amount it pays in 2009 for ECP in the treatment of Angina by 5.8%, from \$156 per hour for 2008 to \$165 per hour for 2009, a total of \$5,775 for 35 hours of ECP, and Medicare reduced the amount it pays in 2009 for many other therapies.

We plan to use up to \$500,000 of the proceeds of this Offering in 2009-10 for the initial costs of two randomized, controlled clinical studies, one is a two-year, randomized, controlled clinical trial of our ECP and CPD Systems in the treatment of up to 300 Chronic Heart Failure and Angina patients, and the other is a 200 patient, randomized, controlled clinical trial of our ECP System in the treatment of Acute Heart Failure, provided we sell at least \$2.5 million of the Shares being offered. Later, we plan to conduct a new randomized, controlled clinical trial in 200 patients in our ECP System in the treatment of Heart Attacks and Cardiogenic Shock.

We expect to finance the remaining cost of up to \$500,000 for the above described Chronic Heart Failure and Angina clinical trial and the <u>Acute</u> Heart Failure clinical trial from our financial resources and our revenues in 2009 and 2010, although we cannot assure that our resources and revenues will enable us to do

so. If our financial resources and revenues in 2009-2010 are not sufficient to fund the second \$500,000 of cost for this clinical study, the study may have to be terminated and the \$500,000 expended in 2009 may be lost.

We plan to submit the results of these clinical trials, if successful, to Medicare with a request for reimbursement of our ECP System for the treatment of Stable and Acute Heart Failure, for an expansion of reimbursement for our ECP System to all Class II, III and IV Angina patients and for reimbursement of our ECP System in the treatment of Heart Attacks and Cardiogenic Shock. We cannot assure that these clinical trials will be successful or that Medicare reimbursement for any of these conditions will be granted.

#### **Medicare Reimbursement for CPD Tests**

Our CPD System is the only cardiopulmonary diagnostic device that can produce an assessment of a Heart Failure patient's cardiopulmonary condition, with the patient having to step up and down a single step for only 2 to 4 minutes. Other cardiopulmonary diagnostic devices require a Heart Failure patient to perform maximal exercise on a treadmill, which many Heart Failure patients cannot do.

Our CPD System displays the test results numerically and with green (good) or red (bad) bar charts, making it easy for the physician to recognize an abnormal test result. Many other such devices typically display numerical test results only.

Medicare currently pays an average of about \$120 nationally for each test performed on our CPD System and will pay for up to four CPD tests per year for monitoring the condition of Heart Failure patients or Angina patients with Heart Failure. Medicare will also pay for additional CPD tests, to enable a physician to assess the results of adjusting a therapy, such as determining if more hours of ECP are needed, the effect of a different drug dosage or the effect of a different pacemaker setting. A CPD test takes approximately 15 minutes for a trained nurse or technician to perform.

The purpose of the proposed clinical studies of our ECP and CPD Systems in the treatment of Stable Heart Failure and our ECP System in the treatment of Acute Heart Failure in 2009 and 2010 is to obtain Medicare coverage and reimbursement for ECP for the treatment of Stable Heart Failure, expand our Medicare coverage in the treatment of Angina, to establish the ability of our CPD System to determine if more than 35 hours of ECP is necessary to normalize the cardiopulmonary condition of Heart Failure patients, and to obtain Medicare reimbursement of ECP in the treatment of Acute Heart Failure.

We cannot assure that the results of these clinical studies will be successful or, if successful, that these studies will persuade Medicare to grant coverage and reimbursement for ECP in the treatment of these conditions in an amount that will be acceptable to physicians, clinics and hospitals. We believe Medicare's current reimbursement rate of \$165 per hour is attractive to such parties, and we believe it is unlikely that Medicare will choose a reimbursement rate lower than the present amount, although we cannot assure this will prove to be correct.

# Medicare Reimbursement for Sleep Disorder Diagnostic Tests

Our SDD Systems employ advanced devices for the diagnosis and evaluation of therapies of sleep disorders. An estimated 30 million people in the United States suffer from a sleep disorder, but there are only enough existing sleep disorder testing facilities in the United States to treat an estimated 5 million persons annually. A sleep disorder diagnostic test is performed on patients whose sleep questionnaire indicates the potential for a sleep disorder. A sleep titration test is performed on those patients found to have a sleep disorder to establish the therapy needed to treat the sleep disorder. An estimated 80% of those who have a sleep diagnostic test need a sleep titration test.

Medicare currently pays an average of about \$850 nationally for a sleep disorder <u>diagnostic</u> test to determine if a person is suffering from a sleep disorder. The test is performed by a trained sleep technician at night in a specially equipped room in a physician's office, clinic or hospital outpatient department while the

person is asleep (See "Per Hour Per Test Rental Programs"). Many states require a sleep technician to pass a written examination and be licensed.

Medicare currently pays an average of about \$950 nationally for a sleep disorder <u>titration</u> test on persons who have been diagnosed with a sleep disorder to determine what therapeutic device or other medical procedure may be needed to treat their sleep disorder. This test is likewise performed by a trained sleep technician on a different night in the same type of room in a physician's office, clinic or hospital outpatient department, while the person is asleep.

Insurance companies typically pay about 10% to 20% more than Medicare for such sleep diagnostic and titration tests, HMOs pay about the same as Medicare, and uninsured persons generally pay about the same as Medicare.

## Per Hour and Per Test Rental Programs

The principal market for our ECP, CPD and SDD Systems is presently in physicians' and group practice's offices, as these devices are used to treat patients and perform diagnostic tests on an outpatient basis. Our ECP System is used to treat Angina and Heart Failure patients for one hour per day, five days per week for seven weeks. Treatment in a physician's office is more convenient and generally entails less paperwork and waiting time than in a clinic or hospital's outpatient department. If and when Medicare coverage and reimbursement for ECP in the treatment of hospitalized patients with <u>Acute</u> Heart Failure, Heart Attacks and/or Cardiogenic Shock is obtained, hospitals will become a significant market for our ECP Systems.

Physicians are not accustomed to purchasing \$30,000, \$100,000 to \$120,000 pieces of equipment for use in their offices. Leasing, with interest costs over a 5-year period, increases the overall outlay by 40% or more, depending on then current interest rates. Equipment leases are typically non-cancelable and are financed by the credit of the physician or physicians, based on their income tax returns and personal financial statements. Many physicians are reluctant provide this information and do not want to be bound by long term, non-cancellable leases.

Hospitals and clinics are also reluctant to purchase expensive equipment, as many have limited capital equipment budgets and credit lines, and leasing increases the cost of the equipment. As a result, we have found it difficult to sell or lease a sufficient number of our products to physicians for use in their offices or to clinics or hospitals for use in their outpatient departments causing us to incur losses over the previous years.

Since we have confidence in both the patient benefits of our products, based on our clinical trial results described above, and we have confidence in the profitability to physicians, group practices, clinics and hospitals from the use of our products, based on current Medicare reimbursement rates, our solution is to rent our ECP, CPD and SDD Systems by the hour or by the test to physicians, group practices, clinics and hospitals under Rental Agreements that can be terminated by the renter on two or three months prior written notice, with minimum monthly payment amounts. Removing the large up-front cost and the fear of a long-term commitment eliminates the most significant impediments to a physician, group practice, clinic or hospital trying our products, seeing the patient benefits and learning what profits our products might produce for them.

Since cardiologists, internists, GPs and family practitioners are not trained in medical school or residency training programs to use our ECP, CPD or SDD Systems and do not know how to train their nurses or technicians to operate them, we plan to provide a trained operator (nurse of technician) and include his or her cost in the per hour or per test rental charges and minimum monthly payments for our products to some physicians and group practices, making it easy for them to provide the benefits of our ECP, CPD and SDD Systems to their patients. If we do not provide an operator, the per hour and per test charges and the minimum monthly payments will reflect the absence of this cost.

We plan to recruit and train nurses and technicians to use our ECP and CPD Systems and recruit trained sleep technicians to operate our SDD Systems, in both cases from established schools that offer such training and assist their graduates in obtaining licenses and jobs.

In the case of SDD Systems, in addition to sleep diagnostic devices and TV monitors, we provide pull-down Murphy-type beds to convert an exam room to a sleep disorder testing room at night. Each sleep technician is expected to be able to monitor three patients while they are sleeping and being tested.

A majority of the net proceeds from the sale of the Shares being offered are expected to be used to purchase components and assemble our ECP Systems, purchase CPD and SDD Systems and rent them with or without a trained operator to physicians, group practices, clinics and hospitals in the U.S. (and in foreign countries without a trained operator) for a per hour or per test rental charge under 60 or 84 Month Rental Agreements that can be cancelled on two of three months prior written notice, with monthly minimums. If we do not provide an operator, the per test and per hour charges and the monthly minimums will reflect the absence of this cost.

While we presently have no arrangements to borrow from any banks or finance companies, if additional equity (stock) financing is not available to us in the future, we may pledge the products being rented or the rental stream from our Rental Agreements to lenders and borrow the cost of providing the products and the operator under our Rental Agreements. Borrowing entails both the cost of interest and the risk of defaults, which could place the Company's assets at significant risk in the event of a default on any such loans.

Renting our ECP, CPD and SDD Systems with a cancellation privilege also entails the risk of premature cancellation of our Rental Agreements and the return of more ECP, CPD and SDD Systems than we can rent or sell to others. If such occurs, our working capital may be impaired, we may be faced with defaults on borrowings and our ability to continue in business may be jeopardized.

Our proposed Rental Agreements require the physician, practice or hospital to pay us for a minimum number of hours of use each month or a minimum number of tests each month, to assure that the cost of the operator is covered and the System will not go unused. The dollar amount of the minimum number of hours or tests per month is designed to pay the cost of the operator and is expected to return our cost for the System in about ten to twelve months.

In addition, our proposed Rental Agreements will require the physician, group practice, clinic or hospital to pay us a substantial financial penalty if the renter cancels the Rental Agreement, returns our product and buys, leases or rents a comparable product from a third party. The proposed Rental Agreements will also require the physician, group practice, clinic or hospital to grant us the right of first refusal to supply any additional products of the same type they wish to buy, lease or rent in the future.

While we expect the usage of each of our products will equal or exceed the required minimum number of hours or tests per month, we cannot assure that this will happen. However, even at the required minimum number of hours or tests per month, we estimate our return will be significantly larger than if we sold or leased our products.

There are an estimated 170,000 cardiologists, internists, family practitioners and general practitioners in the United Sates who treat Angina and Heart Failure and are potential candidates for the purchase, leasing or rental of our products. For example, if 1% or 1,700 of these physicians were to rent one of each of our ECP, CPD and 3 Bed SDD Systems with two of our operators, at our proposed minimum monthly per hour and per test rental payment rates, this would produce over \$30 million of revenues per month or more than \$360 million per year. However, we cannot assure we will ever be able to rent such number of our Systems with operators to such numbers of physicians in the United States at our proposed rental rates.

Since our Rental Program is new, the per hour or per test rental charges, the monthly minimum number of hours or tests required, our manufacturing or OEM costs and our sales costs may change significantly over time, and other unanticipated costs may occur, which may adversely affect the profitability of our Rental Program. Furthermore, there is no assurance we will be able to successfully rent any significant number of our Systems, that we will not have excessive cancellations of our Rental Agreements and returns of products, which we may be unable to sell, lease or rent to others, or that our Rental Program will be profitable to us.

#### Sales and Rentals

We presently sell our ECP and CPD Systems and, following the completion of this Offering, we also plan to begin renting these products and our SDD Systems through "straight commission" independent sales representatives ("Sales Reps") and Sales Rep Organizations in the United States and through distributors in foreign countries, all of whom represent other manufacturers of medical products and devote only a portion of their time to selling and renting our products.

While reimbursement for the use of medical devices in foreign countries is significantly less than in the United States, and is non-existent in some countries, Angina, Heart Failure and Heart Attack patients outside the United States have less access to new technologies to treat their condition. Virtually all of our sales to foreign distributors are expected to be made pursuant to letters of credit or wire transfers of funds payable in U.S. dollars. As a result, we do not expect to be subject to foreign currency risks.

We usually maintain an inventory of our products and ship the products within days of receipt of a purchase order. As a result, we typically have no order backlog.

#### Field Service

We presently employ a VP Manufacturing, R&D & Field Service who manages the manufacturing of our ECP Systems, the development of new products and the field servicing of our products in the United States. We also provide field services under extended service contracts after the expiration of the original one-year warranty we provide on our products. We also sell parts and charge for the time and travel cost of our field service technicians when they repair our products in the United States after the initial one-year warranty period has expired.

Our distributors are responsible for servicing (repairing and maintaining) our products outside the United States. Our distributors' service technicians are trained to service our products at our factory or at their offices in foreign countries in 4-5 day training courses. We provide parts to our distributors to replace defective parts of products during their one-year warranty period. We also sell parts to our distributors for resale to customers outside the United States whose one-year warranty has expired.

# **Government Regulation**

All of our products are, and will in the future, be subject to extensive governmental regulation and supervision, principally by the FDA and comparable governmental authorities in other countries. The FDA regulates the introduction, advertising, manufacturing practices, labeling and record keeping of all drugs and medical devices. The FDA has the power to seize adulterated or misbranded devices, require removal of devices from the market, enjoin further manufacture or sale or devices and publicize relevant facts regarding devices.

Prior to the sale of any of our products, we are required to obtain marketing approval for each product from the FDA and comparable authorities in foreign countries. Extensive clinical (human) testing of each product, which is both costly and time-consuming, may be required to obtain such approvals. Our business would be adversely affected if we were unable to obtain such approvals or to comply with continuing regulations of the FDA and other governmental agencies. In addition, we cannot predict whether future changes in FDA or foreign government regulations might increase the cost of conducting our business or affect the time required to develop and introduce new products. Specific areas of regulation by the FDA and other related matters are described in detail below:

# **Investigational Device Exemption**

Before a new medical device may be used for investigational research (clinical trials) in the United States, an Investigational Device Exemption ("IDE") application must be approved by the FDA, unless the device has already been cleared for sale by the FDA. Also, to obtain an IDE, the sponsor of the investigational research must first obtain approval for the research from the institutional Review Board ("IRB") of the institution (e.g. hospital, clinic, physician practice, etc.) at which the clinical study is to be conducted.

# 510(K) Premarket Notification

The procedure for obtaining clearance from the FDA to market a new medical device can involve many steps, such as IDE's and PMA's (see "Premarket Approval" below). However, if a device is substantially equivalent to a product marketed prior to May 28, 1976, or is substantially equivalent to a comparable product cleared for sale by the FDA under a 510(k) Premarket Notification, a 510(k) Premarket Notification may be filed to establish the device's equivalence.

The FDA's review process for a 510(k) Premarket Notification can take three months or longer. However, if additional testing or data are requested by the FDA, the overall review process may be extended.

Our current products were cleared for sale in the United States by the FDA pursuant to 510(k) Premarket Notifications. While 510(k) Notifications usually do not require clinical trials, in some cases, 510(k) Notifications may require clinical trials.

### Premarket Approval

Under the Medical Device Amendments of 1976, all medical devices are classified by the FDA into one of three classes. A "Class I" device is one that is subject only to general controls, such as labeling requirements and good manufacturing practices ("GMP"). A "Class II" device is one for which general controls and performance standards alone are insufficient to secure safety and effectiveness, unless the device qualifies for sale under a 510(k) Premarket Notification. "Class III" devices generally require clinical testing to establish their safety and efficiency in treating specific diseases or conditions, and either a 510(k) Premarket Notification, with or without a clinical trial, or a Premarket Approval ("PMA") with a clinical trial. An application for the intended use of the device must be approved by the FDA before the device can be marketed in the United States. A device is generally classified as a Class I, II or III device based on recommendations of advisory panels appointed by the FDA. Our ECP System is presently considered a Class III device eligible for marketing under a 510(k) Premarket Notification. However, the FDA can change any Class III device's classification to require a PMA application at any time.

The filing of a PMA Application generally entails one or more expensive, lengthy clinical trials. After completion of the clinical trials, a rigorous review of the data and an inspection of the manufacturing facility and process by the FDA can take one year or longer, unless additional testing or data are requested by the FDA, in which case the review process can be considerably longer.

We cannot assure that PMA approvals will not be required by the FDA for our current products or, if PMA approvals are required, that they can be obtained or, if obtained, that they can be maintained. The failure to obtain and maintain PMA approvals for any of our products, if required, could have a material adverse effect upon our future operations.

# Inspection of Plants

The FDA also has authority to conduct detailed inspections of manufacturing plants to determine whether or not the manufacturer has followed its GMP requirements, which are required for the manufacture of medical devices. Additionally, the FDA requires reporting of certain product defects and prohibits the domestic sale or exportation of devices that do not comply with the law. We believe we are in compliance in all material

respects with these regulatory requirements, and we expect that our processes and procedures in place will satisfy the FDA, although we cannot assure that this will be so.

### State Regulation

Federal law preempts states or their political subdivisions from regulating medical devices. Upon application, the FDA may permit state or local regulation of medical devices which is either more stringent than federal regulations or is required because of compelling local conditions. To date, and to the best of our knowledge, only California has filed such an application. On October 5, 1980, the FDA granted partial approval to such application, effective December 9, 1980. The California requirements, which have been exempted from federal law preemption, have not had a materially adverse effect on us to date.

### **Insurance Reimbursement**

To permit the users of our products to obtain reimbursement under Federal health care programs such as Medicare, we may be required to demonstrate, in an application to the Centers for Medicare and Medicaid Services ("CMS"), which administers the Medicare and Medicaid Programs, at either the state or federal level or both, the safety and efficacy of our products and the benefit to patients therefrom which justify the cost of such treatment. There is no assurance that any application for coverage and reimbursement by us will be approved by CMS. Most private health insurance companies, health maintenance organizations ("HMOs") and state health care programs have standards for reimbursement similar to those of CMS and usually follow CMS' coverage decisions. If any of our products is refused reimbursement by Medicare, private insurers, HMOs and/or health care programs, sales and rentals of such product would be adversely affected.

# Cost of Compliance With FDA and Other Applicable Regulations

The costs of complying with FDA and other governmental regulations prior to the sale of our products are reflected mainly in our R & D and clinical trial expenditures. The cost of first obtaining an IDE for a product, if required and, after having developed and clinically testing a product to assure it is safe and effective, obtaining approval of a PMA or 510(k) Premarket Notification therefor, as well as making an application to CMS in order to obtain Medicare coverage its use, adds significantly to the cost of developing and bringing a medical device to the market over what such cost would have been if such regulatory requirements did not exist.

Compliance with regulatory requirements also lengthens the time required to develop and commence marketing a product. These delays increase our R & D costs by (a) lengthening the time during which we must maintain and bear the carrying costs of a given research and development effort and (b) delaying the time when we can commence realizing revenues from sales of a product, during which time we must continue to bear administrative and overhead costs. It is, however, not possible for us to quantify or estimate in advance the direct and indirect costs of complying with such regulatory requirements, particularly since the expense and difficulty of such compliance can vary greatly, depending upon the nature of the product, its intended use, the technological success of the R & D effort and the results of animal and/or human clinical testing of the product.

In the event applicable regulations require more rigorous testing than might otherwise be deemed necessary, the costs of testing the product by unaffiliated institutions (and fees or royalties, if any, payable to them) may be deemed in part a cost to us of compliance with such regulatory requirements.

# **Employees**

On December 31, 2008, we had eight employees, of whom three were employed in production and engineering, one in accounting, one in marketing and three in general and administrative functions. Our employees are not subject to any collective bargaining agreements, and we believe our relationship with our employees is good.

We may require additional employees in the areas of administration, product development, research, production, regulatory affairs, accounting, sales and marketing in the future. There is intense competition for capable, experienced personnel in the medical device field, and we cannot assure that we will be able to obtain new qualified employees when required. Management believes its relations with its employees are good.

### **Patents and Patent Applications**

We own U.S. Patent, No. 7,244,225, covering our Graduated™ Low Pressure ECP Regimen for treating Heart Failure and other medical conditions and improvements in our ECP Systems, and another U.S. Patent, covering an advanced Graduated™ Low Pressure ECP Regimen for the treatment of Stable (chronic) Heart Failure, has been allowed by the U.S. Patent Office and is expected to issue in April or May 2009.

We cannot assure that (a) any Patents will be issued from any patent applications we have filed or may file in the future, (b) any issued Patents will prove enforceable, (c) we will derive any competitive advantage from any issued Patents or (d) our products may not infringe Patents owned by others, licenses to which may not be available to us or available at an acceptable cost, in which event, we may be faced with patent litigation, which is extremely costly and may entail damages, judgments and settlements and may require us to abandon the sale of the infringing or allegedly infringing products. To the extent that pending patent applications do not issue, we may be subject to more competition. The issuance of Patents on some but not all aspects of a product may be insufficient to prevent competitors from essentially duplicating the product by designing around the patented aspects. We are not obligated to pay royalties under our issued U.S. Patent and pending patent application, which have been assigned to the Company without cost. If we should acquire licenses to Patents or patent applications in the future, we may be obligated to pay royalties or other payments to their owners.

### Competition

We face competition from a number of small companies that import ECP devices from China or assemble ECP devices made wholly or partially of parts from China or acquired elsewhere. Among the small companies with which we compete are Vasomedical, Inc., American Cardiology Systems, Inc., ScottCare, Inc. and others, certain of which are publicly held. While our ECP Systems compete with these companies on published clinical benefits, price, features and service, none of these companies have clinical studies published in peer-reviewed medical journals demonstrating clinical benefits comparable to ours. Also, to our knowledge, none of these companies offers a per hour or per test rental program, with or without trained operators, comparable to ours.

We also compete with large, established, publicly-held companies in the medical field, which manufacture cardio pulmonary diagnostic devices and sleep disorder testing equipment and supplies. The larger of such established companies include Respironics, ResMed, Mallinckrodt, Compumedics, Viasys, Nellcor and Embia, all of which have greater financial resources, R & D and manufacturing facilities, technical skills, management staffs and sales and marketing organizations than us.

### Insurance

We have a commercial general liability insurance policy and a products liability insurance policy, each providing coverage per claim and in the aggregate of \$5,000,000. While we have never had to report an adverse effect from our ECP Systems to the FDA, we cannot assure this amount of insurance will be sufficient to protect our assets against claims by patients, users of our products or others. Although there have been no successful claims against us in the past, there is no assurance we will be able to maintain such liability insurance in force in the future at an acceptable cost, or at all, in which case our assets would be at risk in the event of successful claims against us. Court awards in excess of the amount of insurance then in force could have a serious adverse affect upon our financial condition and future viability. We do not carry any directors and officers liability insurance, but our By-Laws contain indemnification agreements covering our officers and directors.

### **Properties**

We currently occupy approximately 14,000 square feet of modern office, manufacturing and warehouse space in Irvine, CA, which we lease at a rental of approximately \$24,000 per month. We sublease approximately 8,000 sq. ft. of space in this building on a month-to-month basis at a small premium over our monthly rental cost for this area to an unaffiliated party. Our present facilities are capable of manufacturing several times our current volume of products, and we can more than double the size of our facility if we choose to terminate the month-to-month rental of 8,000 sq. ft. of space by our sub-tenant. Our lease expires in January 2010. Management considers all of its facilities to be well maintained and adequate for its purpose.

### Litigation

There are presently no lawsuits against us and none are threatened. We may be subject in the future to various lawsuits that may arise in the ordinary course of our business. The litigation process is costly, time consuming and inherently uncertain, and it is possible that the resolution of any future litigation may materially adversely affect our business and financial condition.

### **MANAGEMENT**

### Officers And Directors

<u>Name</u>	<u>Age</u>	<u>Position</u>
Marvin P. Loeb	82	Chairman and CEO
John McCallum	44	President, COO & Director
Robert J. Sullivan	67	V. P. – Manufacturing
Lorrie L. Stratton	57	Secretary/Treasurer
Donald Baker	79	Director
Thomas R. Ulie	60	Director
Glenn D. Yeik	42	Director

Marvin P. Loeb has been Chairman, CEO and a Director of our Company since 1986. He has been the Chairman of the Board of Directors of Trimedyne, Inc. since 1980, a publicly-held manufacturer of medical lasers. Since November 1988, he has been Chairman of Ultramedics, Inc., a privately held company whose principal interest is its investment in the Company. Dr. Loeb has been President of Master Heath Services, Inc., a family held medical consulting firm, since 1973, and Marvin P. Loeb and Company, a family held patent licensing firm, since 1983. Dr. Loeb holds an honorary Doctor of Science Degree from Pacific States University and a Bachelor of Science Degree from the University of Illinois.

John McCallum has been President, COO and a Director of our Company since April 1, 2004. Prior thereto he was Vice President of Business Development & International Sales and Marketing from August 2001 to March 2004 of Cortex Biophysik, GmbH of Germany; Asia Pacific Sales Manager from July 1999 to July 2001 of Sensormedics, Inc. (now Viasys); Vice President of Sales and Marketing from October 1996 to June 1999 of Compumedics, Pty., Ltd. Of Australia; and Director of Sales for Asia Pacific and Latin America from July 1992 to October 1996 of Medical Graphics Corp. Mr. McCallum has extensive experience in the Pulmonary, Cardiology and Sleep markets throughout the U.S., Asia, Europe and Latin America for more than 17 years. Mr. McCallum graduated from Manchester Metropolitan University in the UK with an Honors Degree in Biological Sciences.

Robert Sullivan has been with the Company since December 2001, initially as Manufacturing Manager and was elected to his present position as Vice President, Manufacturing, in April 2003. Prior thereto, Mr. Sullivan was employed by Nobel Biocare from December 1999 to December 2001 and by Chiron Vision from January 1985 to July 1998, where he served in several capacities dealing with product development, sales support and training. He has been engaged in electronic medical device development since 1970.

Lorrie Stratton has been employed by the Company for approximately 55% of her time as Accounting Manager from July 1996 to June 30, 2008, and thereafter as Chief Accounting Officer. Prior thereto, she was our Controller from 1989 to July 1996. Mrs. Stratton graduated with a Bachelor of Science Degree in Business Administration from California State Polytechnic University, Pomona, California.

Glenn D. Yeik has been a Director of our Company since October 2004. He has been President, Chief Operating Officer and a Director of Trimedyne, Inc. since September 2003. Prior thereto, he was Executive Vice President of Trimedyne, Inc. from April 2002 to September 2003 and Vice President of Product Development from March 2000 to April 2002. Mr. Yeik was Manager and Director of Electronic Systems at AngioTrax, Inc. from May 1998 to March 2000. Mr. Yeik was employed as an Engineering Manager of Trimedyne, Inc. from August 1992 to May 1998. Prior thereto, Mr. Yeik was a Software Engineer at Cardiac Sciences, Inc. from June 1991 to August 1992. Mr. Yeik received a Bachelor of Science Degree in Electrical Engineering from LeTourneau University. Mr. Yeik is Dr. Loeb's son-in-law.

Donald Baker has been a director of our Company since 1992. He also has been a Director of Trimedyne, Inc. since 1983. Mr. Baker retired after 39 years as a Capital Partner of the law firm of Baker & McKenzie. He holds a J.D.S. degree from the University of Chicago Law School. Mr. Baker was a Director of the management committee of the Mid-America Committee of Chicago for many years, and has been a director of various medical technology companies. He is a member of the Chicago and American Bar Associations.

Thomas R. Ulie has been a director of our Company since 2005. He is a Chartered Financial Analyst, has been in the investment field for more than 30 years, and has been CEO of First Island Capital, Inc., a West Coast-based investment firm since 1994. Mr. Ulie also serves as a Director of a number of medical companies and has wide-ranging experience in the investment community, having worked in money management, research and investment banking. Prior to First Island Capital, Mr. Ulie served as Senior Managing Director for the Stanford Company, a NYSE member firm. Earlier, Mr. Ulie was an Associate Director of Bear Stearns and a member of the New York Stock Exchange Hearing Board, an analyst for Lehman Brothers, Fiduciary Counsel Inc. and the Commodity Exchange Authority. He was Director of the Mercer Island Rotary Club from 2006 to 2008.

The Company has made no loans to, has no retirement plan for and carries no key man life insurance on any of its officers, directors or employees. To our knowledge, none of the Company's officers, directors or employees was an executive officer, director or partner in any entity which filed under the Bankruptcy Act or any State insolvency law.

# **Executive Compensation**

The following table set forth the executive compensation paid during the years ended December 31, 2007 and 2008 to our executive officers who earned more than \$100,000 in combined salary, stock option awards and other compensation in such years.

Compensation		Annual Compensation (1)		Securities Underlying	All Other	
Name of Individual And Principal Position	Year 	Salary \$ 	Bonus \$ 	Options \$ Shares)	Compensation (\$) (2)	
John McCallum President and Chief Operating Officer	2008 2007	\$126,877 \$ 98,405	\$ 0 \$ 0	0 \$1,000,000	\$7,754 \$6,923	

# **Security Ownership Of Management And Others**

We presently have 7,427,060 Shares outstanding, with 11,166,960 Shares outstanding on a fully diluted basis. The following table sets forth the name and address of each beneficial owner of more than five percent of the Company's Common Stock on a fully-diluted basis known to the Company, by each director of the Company, by each named executive officer, and by all directors and executive officers as a group, the number of shares beneficially owned by such persons as of December 31, 2008 and the percent of the class so owned. Each person named in the table has sole investment and sole voting power with respect to the number of Shares set forth opposite his name, except as otherwise indicated. All shares are directly owned.

Title of Class	Name and Address of Beneficial Owner	Amount Held and Percent of Share Outstanding on a Fully-Diluted Basi	
•	Major Shareholder		
Common Stock \$.01 Par Value	Marvin P. Loeb, Chairman & CEO (1) 25901 Commercentre Drive Lake Forest, CA 92630	6,062,102	54.3%
	Other Directors and Executive Officers		
	John McCallum, President & COO (2) 18872 Bardeen Avenue Irvine, CA 92612	520,000	4.7%
	Robert J. Sullivan, V.P. Manufacturing (3) 18872 Bardeen Avenue Irvine, CA 92612	50,000	0.4%
	Lorrie L. Stratton, Treasurer & CAO (4) 18872 Bardeen Avenue Irvine, CA 92612	100,000	0.9%
	Donald Baker, Director (5) 544 Earlston Road Kenilworth, IL 60043	391,694	3.2%
	Thomas R. Ulie, Director (6) 8843 SE 77 <sup>th</sup> Place Mercer Island, WA 98040	1,014,449	9.1%
	Glenn D. Yeik, Director (7) 25901 Commercentre Drive Lake Forest, CA 92630	82,500	0.7%
	All Directors and Executive Officers as a Group (7 persons)	8,190,745	73.3%

<sup>(1)</sup> Consists of 3,672,102 Shares owned by Dr. Loeb and his wife, adult children, grandchildren and trusts for their benefit, of which Dr. Loeb is not a beneficiary, 2,340,000 Shares issuable to Dr. Loeb

and his designees in the event of the conversion of \$900,000 of Notes and accrued interest to maturity, and 50,000 Shares issuable to Dr. Loeb in the event of his exercise of stock options.

- Consists of options to purchase 520,000 Shares. (2)
- Consists of Options to purchase 50,000 Shares. (3)
- Consists of Options to purchase 100,000 Shares. (4)
- Consists of 126,694 Shares owned, 130,000 Shares issuable in the event of Conversion of Notes (5) and accrued interest to maturity, options to purchase 95,000 Shares and Warrants to purchase 10,000 Shares.
- Consists of 816,999 Shares owned, 130,000 Shares issuable on Conversion of Notes and accrued (6)interest to maturity, 40,000 Shares issuable on exercise of Warrants and options to purchase 27.500 Shares.
- (7) Consists of 55,000 Shares owned and options to purchase 27,500 Shares.

### **Stock Option Grants to Executive Officers and Directors**

INDIVIDUAL CDANTS

During the year ended December 31, 2008, we did not grant any options to our officers or employees. In 2007, we granted options to purchase 400,000 Shares to John McCallum, an option to purchase 50,000 Shares to Lorrie L. Stratton, and options to purchase 15,000 Shares to each of our four non-management Directors, Donald Baker, Richard F. Horowitz (now deceased), Thomas R. Ulie and Glenn D. Yeik, all of which options are exercisable at a price of \$2.50 per Share.

On December 31, 2008, we had outstanding stock options to purchase 1,088,000 Shares at prices from \$2.35 to \$2.50 per Share, of which options to purchase 603,000 Shares were then exercisable. In order to obtain and retain capable and experienced officers, directors and employees, we plan to grant additional stock options in the future at prices related to the price of the Shares in this Offering or, thereafter, at the then market price of our Shares.

The following table provides information concerning grants of options during the year ended December 31, 2007 to the named executive officers and directors.

	INDIVIDUAL GRANTS			
<u>NAME</u>	NUMBER OF SECURITIES UNDERLYING OPTIONS GRANTED <sup>(1)</sup>	PERCENT OF TOTAL OPTIONS GRANTED IN 2007	PRICE (\$/SH)	EXERCISE EXPIRATION DATE
John McCallum	400,000	74.8%	\$2.50	August 14, 2017
Lorrie L. Stratton	50,000	9.3%	\$2.50	August 14, 2017
Donald Baker	15,000	2.8%	\$2.50	August 30, 2013
Richard F. Horov	vitz <sup>(2)</sup> 15,000	2.8%	\$2.50	April 30, 2013
Thomas R. Ulie	15,000	2.8%	\$2.50	April 30, 2013
Part II, Form 1-A	BC 3.28.09	35		

(1) Stock options granted to our officers and employees under our Option Plan vest 20% per year over 5 years and are exercisable over a 10-year period. Stock options granted to our non-management directors are issued under our Directors' Stock Option Plan, vest one-third each year over a 3-year period and are exercisable over a 6-year period. The above options were granted at \$2.50 per share, the price of the Company's most recent private placement to unaffiliated investors.

(2) A director until his death in September 2008.

Under the Directors' Option Plan, our non-management directors each a receive an option to purchase 15,000 Shares on each anniversary date of their having served as a Director for three (3) years at the most recent private offering price to unaffiliated investors or, if public, the closing price per Share on the date of the grant.

### TRANSACTIONS WITH MANAGEMENT

The following are transactions from June 1, 2006 through December 31, 2008, in which certain of our officers or directors had a direct or indirect material interest. The Company believes that the terms of the transactions described below are as favorable as could have been obtained with unaffiliated third parties.

From June 1, 2005 through December 31, 2008, our Chairman and Chief Executive Officer loaned us an aggregate of \$900,000, which is evidenced by \$900,000 of 6% Senior Convertible Secured Notes ("Notes"). The Notes are convertible, with accrued interest, into Shares at a price of \$0.50 per share until their maturity from 2011 through 2013.

During the same period, Donald Baker and Thomas R. Ulie, directors of the Company, similarly each loaned us \$50,000, evidenced by \$50,000 of Notes, respectively. These Notes are convertible, with accrued interest, into Shares at a price of \$0.50 per Share from 2010 to 1011.

Dr. Loeb, our Chairman and CEO, was issued without cash consideration, 720,000 Shares for serving without cash compensation from January 1, 2006 through December 31, 2008.

Richard F. Horowitz died in September 2008. Prior thereto, he was a director of the Company, and was a member of the firm of Heller, Horowitz & Feit, P.C., counsel to the Company. During the year ended December 31, 2008, we incurred \$0 of legal fees and costs as a result of the above law firm acting as our counsel.

### **DESCRIPTION OF SECURITIES**

Our authorized capital stock consists of 40,000,000 shares of Common Stock, par value \$.01, and 1,000,000 shares of Preferred Stock.

### **Preferred Stock**

No shares of our Preferred Stock are presently outstanding. Our Board of Directors has the right to fix the rights and preferences of any of our Preferred Stock which might be issued in the future, without obtaining approval of our Shareholders. Such rights and preferences could include the Preferred Stock having preference over the common stock in the event of liquidation of the Company, a greater number of votes per share, conversion into common stock at a preferable rate, a fixed or preferential dividend rate per share and others.

### Common Stock

The shares of our common stock presently outstanding, and any shares of our common stock issued pursuant to this Offering, upon conversion of the Notes or the exercise of stock options or Warrants will be fully paid and non-assessable. Each holder of common stock is entitled to one vote for each share owned on all matters voted upon by stockholders, and a majority vote is required for all actions to be taken by stockholders. In the event we liquidate, dissolve or wind-up our operations, the holders of our common stock are entitled to share equally and ratably in our assets, if any, remaining after the payment of all our debts and liabilities and the liquidation preference of any then outstanding Convertible Notes and shares of Preferred Stock.

Holders of our common stock have no preemptive rights and no cumulative voting rights, and no redemption, sinking fund, or conversion provisions. Since the holders of common stock do not have cumulative voting rights, holders of more than 50% of the outstanding shares of common stock can elect all of our Directors, and the holders of the remaining shares by themselves cannot elect any Directors.

Holders of our common stock are entitled to receive dividends, if and when declared by the Board of Directors out of funds legally available for such purpose, subject to the dividend and liquidation rights of any Convertible Notes or Preferred Stock that may then be outstanding.

### Warrants

We presently have 536,900 Warrants outstanding which are exercisable until June 30, 2009, to purchase 536,900 Shares at a price of \$3,75 per Share. These Warrants were issued in connection with our earlier sale of Shares in units ("Units") of two (2) Shares and one Warrant at a price of \$5.00 per Unit. These presently outstanding Warrants do not contain any anti-dilution provisions.

### **Convertible Notes**

The Convertible Notes and any of this class of Convertible Notes we may sell in the future have antidilution provisions, are secured by all of the assets of the Company and will have preference to the assets of the Company over the Common Stock and Preferred Stock, if any, in the event of the dissolution or liquidation of the Company. The Convertible Notes bear interest at 6% per annum and are convertible, along with any accrued interest, into Shares at any time prior to maturity at \$0.50 per Share.

### Anti-Dilution Rights of Certain Shareholders

The presently outstanding Convertible Notes contain anti-dilution provisions, which may require the Company to reduce the exercise price or conversion rate if it issues Shares at a price less than the conversion price of the Convertible Notes and in certain other circumstances.

If any or all of the Shares being offered are sold by broker/dealers, the warrants issued to them may contain similar anti-dilution provisions.

As a result of the above anti-dilution provisions, we may be required to issue an undeterminable number of Shares, which could significantly dilute the percentage of ownership in the Company of the purchasers of the Shares being offered.

### Reports to Shareholders

We plan to furnish annual reports to our shareholders, which may include audited or un-audited annual financial statements, or we may post these reports on our website, www.Cardiomedics.com. If prepared, we may also provide un-audited quarterly financial statements and periodic progress reports to shareholders or post them on our website. We are a not reporting company under the Exchange Act of 1934, as amended (the "Exchange Act").

### **Transfer Agent**

The transfer agent and registrar for our Shares is expected to be American Stock Transfer and Trust Company, 40 Wall Street, New York, New York.

# THE COMMISSION'S POLICY ON INDEMNIFICATION

Article 12 of our Certificate of Incorporation contains provisions for the indemnification of our directors and officers to the fullest extent permitted by Nevada law.

Section 78.751 of the Nevada Revised Statutes, as amended, authorizes us to indemnify any director or officer under certain prescribed circumstances and, subject to certain limitations, against certain costs and expenses, including attorneys' fees actually and reasonably incurred in connection with any action, suit or proceeding, whether civil, criminal, administrative or investigative, to which the director is a party by reason of being our director or a director of our subsidiary, if it is determined that the director acted in accordance with the applicable standard of conduct set forth in those statutory provisions.

We may also purchase and maintain insurance for the benefit of any director or officer that may cover claims for which we could not otherwise indemnify him or her.

Insofar as indemnification for liabilities arising under the Act may be permitted to our directors, officers and controlling persons pursuant to the foregoing provisions, or otherwise, we have been advised that it is the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Act and is, therefore, unenforceable.

### SHARES AVAILABLE FOR FUTURE SALE

Of the 7,427,060 Shares outstanding at December 31, 2008, all of which have been held by the holders for more than six (6) months, 2,756,265 Shares presently held by non-controlling parties may be sold pursuant to Rule 144 of the Securities and Exchange Commission, and 4,670,795 Shares presently held by our executive officers, directors and controlling shareholders may be sold pursuant to Rule 144, subject to limitations on the number of Shares which may be sold by such parties during certain periods.

### **TAX CONSEQUENCES**

The Company is a "C" corporation and is not an "S" or "LLC" corporation or a partnership. As a result, investors in the Shares will have no tax consequences due to the losses or profits, if any, of the Company. However, purchasers of the Shares may have tax consequences from dividends or distributions, if any, or in the event of the merger or acquisition of the Company, the liquidation or dissolution of the Company or in other events.

PROSPECTIVE INVESTORS IN THE COMPANY SHOULD CONSULT THEIR ACCOUNTANTS AND/OR TAX ADVISORS WITH RESPECT TO ANY POSSIBLE FEDERAL, STATE OR LOCAL TAX CONSEQUENCES WHICH MAY ARISE AS A CONSEQUENCE OF AN INVESTMENT IN THE COMPANY.

### **LEGAL MATTERS**

In connection with this offering, J. Holt Smith of the law firm of Smith & Associates, 411 Santa Monica Blvd., Suite 3, Los Angeles, CA 90401, has given its legal opinion that we are in good standing in the State of Nevada with due authority to conduct our business, the Shares offered under this Offering Circular have been duly and validly authorized and the Shares will be, when issued, fully paid and non-assessable. A copy of this opinion is filed as an Exhibit to the Registration Statement of which this Offering Circular is a part.

### **AVAILABLE INFORMATION**

Upon completion of this Offering, we may be subject to the information requirements of the Securities Act, which may require us to file reports, proxy statements and other information with the SEC. Copies of any reports, proxy statements and other information we may be required to file can be inspected at the Headquarters Office of the Securities and Exchange Commission located at 100 F Street, N.E. Washington, D.C. 20549.

Copies of the material we file may also be obtained from the Public Reference Room of the SEC, at 100 F Street, N.E., Washington, D.C. 20549 at prescribed rates. The Public Reference Room can be reached at (202) 942-8090. The SEC also maintains a web site that contains reports, proxy and information statements and other information regarding us. This material can be found at <a href="http://www.sec.gov">http://www.sec.gov</a>.

### FINANCIAL STATEMENTS

The Financial Statements included in the Offering Circular were prepared internally and have not been audited by an independent accounting person or firm. However, these Financial Statements, in the opinion of the management of the Company, contain all adjustments of a normally recurring nature necessary for a fair statement of the Company's financial condition and its results of operations for the periods indicated.

### INDEX TO FINANCIAL STATEMENTS FOR YEARS 2007 AND 2006

### Financial Statements:

Balance Sheet at December 31, 2008	F-1
Statements of Operations for the years ended December 31, 2008 and 2007	F-2
Statements of Stockholders' Equity for the years ended December 31, 2008 and 2007	F-3
Statements of Cash Flows for the years ended December 31, 2008 and 2007	F-4
Notes to Consolidated Financial Statements	F-5

# BALANCE SHEET At DECEMBER 31, 2008 (Unaudited)

# **ASSETS**

Current Assets Cash and Cash Equivalents Accounts Receivable Inventories Prepaid Expenses & Other Assets Total Current Assets	\$ 117,105 9,726 319,593 52,570 \$ 498,994
Property and Equipment (Net)	\$ <u>218</u>
Total Assets	\$ <u>499,212</u>
LIABILITIES AND STOCKHOLDERS' EQUITY	
Current Liabilities Accounts Payable and Accrued Expenses	\$ 478,538
Total Current Liabilities	\$ 478,538
Long Term Liabilities Notes Payable Convertible Notes Accrued Interest  Total Long Term Liabilities	\$ 20,000 1,000,000 136,866 \$ 1,156,866
Stockholder's Equity Common Stock, 7,427,060 Shares Outstanding Paid in Capital Cost of Invested Funds Retained Earnings Current Year Profit (Loss) To Date	\$ 74,270 8,521,292 (19,000) (9,523,383) (189,371)
Total Liabilities And Equity	\$ 499,212

# STATEMENTS OF OPERATIONS FOR THE YEARS ENDED DECEMBER 31, 2008 AND 2007 (Unaudited)

# **Years Ended December 31**

	2008	2007		
Revenues	\$1,142,289	\$ 860,282		
Cost of Goods Sold:				
Material Cost	174,504	148,997		
Labor and Other Direct Expenses	237,741	211,985		
Total Cost of Goods Sold	\$ 412,245	\$ 360,982		
Gross Profit	\$ 730,044	\$ 499,300		
Expenses Selling Expense General and Administrative Expense Research and Development Regulatory Amortization Total Expenses	296,193 662,275 27,187 0 0 \$ 985,645	185,648 657,533 0 (2,608) 0 \$ 840,573		
Net Income (Loss) From Operations	\$ (259,698)	(341,273)		
Other Expenses Interest Depreciation Prior Year Payables Adjustment	(47,388) (1,665) (120,047)	(44,260) (6,563) 0		
Provision (Benefit) for Income Taxes				
State Income Taxes Federal Income Taxes	(666) 0	(964) <u>0</u>		
Net Profit (Loss)	<u>\$ (189,371)</u>	\$ (393,060)		
Net Profit (Loss) Per Share	\$ (0.03)	\$ (0.05)		
Weighted Average No. of Shares Outstanding **	7,427,060	7,187,060		

# STATEMENTS OF STOCKHOLDERS' EQUITY FOR THE YEARS ENDED DECEMBER 31, 2008 AND 2007 (Unaudited)

# Years Ended December 31

	<u>2008</u>	<u>2007</u>
Balance at Beginning of period	\$(1,066,821)	\$ (793,761)
Share-based Compensation	120,000	120,000
Net Profit(Loss)	(189,371)	(393,060)
Balance at End of Period	\$(1,136,192)	\$(1,066,821)

# STATEMENTS OF CASH FLOWS FOR THE YEARS ENDED DECEMBER 31, 2008 AND 2007 (Unaudited)

# Years Ended December 31

	2008	2007
Net Income:	\$(189,371)	\$(393,060)
Adjustments to reconcile Net Income (Loss) to net cash Provided by (used in) operating activity:		
Stock Based Compensation Accrued Interest on Notes Depreciation	120,000 45,434 1,665	32,311 6,563
Changes in operating assets and liabilities:		
Trade Accounts Receivable Inventories Other Assets Accrued Expenses	109,418 (16,600) 20,155 (380,022)	25,208 87,291 (4,377) (47,772)
Net Cash provided by (used in) operating activities:	(289,321)	(173,836)
Cash Flows from investing activities:		
Purchase of property and equip.	0	0
Net cash used in investing activities	0	0
Cash flows from financing activities:		
Proceeds from Secured Notes	400,000	194,530
Net cash provided by (used in) financing activities	400,000	194,530
Net increase (decrease) in cash and cash equivalents	110,679	20,694
Cash and cash equivalents at beginning of period	6,426	(14,268)
Cash and cash equivalents at end of period	\$ 117,105	\$ 6,426

# CARDIOMEDICS, INC. NOTES TO FINANCIAL STATEMENTS

### NOTE 1. THE COMPANY

Cardiomedics, Inc. ("Cardiomedics" or "the Company") is engaged primarily in the manufacture, sale and servicing (repair) of External Counter Pulsation ("ECP") Systems for the outpatient treatment of severe angina patients and severe angina patients who also suffer from heart failure. In the future, in addition to selling its ECP Systems, the Company plans to focus its efforts on renting them for a per hour charge, with or without an operator, under Rental Agreements that can be terminated on two or three months notice. The Company also sells Cardio Pulmonary Diagnostic ("CPD") Systems and plans to sell Sleep Disorder Diagnostic ("SDD") Systems and to rent them for a per test charge. The Company markets its products in the U.S. and a number of foreign countries. The Company has no subsidiaries.

# NOTE 2. SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

### Cash and Cash Equivalents

The Company considers all liquid investments, with a maturity of three (3) months or less, to be cash equivalents.

### Credit Risk

The Company carries receivables on sales of its products in the United States. Its terms are net 30 days. The Company requires payment by wire transfer or bank letter of credit on sales in foreign countries and, as a result, has no foreign exchange risk. The Company performs limited credit evaluations of its U.S. customers, sometimes requires partial pre-payment, but does not require collateral. During 2008 and 2007, credit losses were not significant.

The Company's bank balances in excess of federally insured limits were not significant at December 31, 2008.

### Inventories

Inventories consist of raw materials and component parts, work-in-process and finished goods. Inventories are recorded at the lower of cost or market, cost being determined principally by use of the standard cost method. Cost is determined at the actual cost for raw materials, and at production cost (materials, labor and indirect manufacturing overhead) for work-in-process and finished goods.

### Goodwill

The Company had no goodwill on its balance sheet at December 31, 2008 or 2007.

# Impairment of Long-Lived Assets

SFAS No. 144, "Accounting for Impairment or Disposal of Long-Lived Assets", requires that long-lived assets, such as property and equipment and purchased intangibles subject to amortization, be reviewed for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable. Recoverability of the asset is measured by comparison of its carrying amount to undiscounted future net cash flows the asset is expected to generate. If such assets are considered to be impaired, the impairment to be recognized is measured as the amount by which the carrying amount of the asset exceeds its fair market value. Estimates of expected future cash flows represent management's best estimate based on currently available information and reasonable and supportable assumptions. Any impairment recognized in accordance with SFAS No. 144 is permanent and may not be restored. To date, the Company has not recognized any impairment of long-lived assets in connection with SFAS No. 144.

### Stock-Based Compensation.

The Company has not granted any stock-based compensation to its officers, directors, employees or non-employees, other than stock options. Being privately held, the Company is not required to account for any stock-based compensation to its officers, directors or employees. See "Stock Options" under NOTE 6.

## Property and Equipment

Property and equipment is carried at cost or fair market value on the date of acquisition. Depreciation and amortization are computed using the straight line method over the asset's expected useful life. The useful life of the Company's property and equipment are:

Machinery & Equipment

5 Years

Software

5 Years

### **Income Taxes**

Income taxes are recognized in the year incurred. Deferred taxes are computed in accordance with existing tax laws.

### Use of Estimates

The preparation of financial statements in conformity with accounting principles generally accepted in the United States of America requires management to make certain estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the reporting period. Actual results could differ from those estimates. Significant estimates and assumptions include inventory valuation, allowances for doubtful accounts and deferred income tax assets, recoverability of goodwill and long-lived assets, and losses for contingencies and certain accrued liabilities.

# Revenue Recognition

The Company's present revenues include revenues from the sale of its products and extended service (warranty) contracts in some cases.

In accordance with Staff Accounting Bulletin 104, "Revenue Recognition," the Company recognizes revenue from products sold once all of the following criteria for revenue recognition have been met: (i) persuasive evidence that an arrangement exists, (ii) the products have been shipped, (iii) the prices are fixed and determinable and not subject to refund or adjustment, and (iv) collection of the amounts due is reasonably assured.

Revenues from the sale of the Company's products are recognized upon shipment and passage of title of the products, provided that all other revenue recognition criteria have been met. Generally, the Company's products are sold "Ex Works, Irvine, CA" and customers are required to insure the goods from the Company's place of business. Accordingly, the risk of loss transfers to the customer once the goods have been shipped from the Company's warehouse. The Company sells its products primarily through commission sales representatives in the United States and distributors in foreign countries. In cases where the Company utilizes distributors, it recognizes revenue upon shipment, provided that all other revenue recognition criteria have been met, and ownership risk has transferred. On sales to distributors, the Company does not have any post shipment obligations such as installation or acceptance provisions. All U.S. sales of the Company's products are sold with a one year warranty which includes parts and labor. All sales of products outside the U.S. are sold with a one year parts only warranty, with the distributor responsible for installation, training and labor in repairing and maintaining the product for one year.

The Company usually maintains an inventory of its products and ships its products within days of receipt of a purchase order. As a result, the Company typically has no order backlog.

# Research and Development Costs

All research and development costs, including licensing costs, are charged to expense as incurred. In accordance with this policy, all costs associated with the design, development and testing of the Company's products have been expensed as incurred.

### Per Share Information

Basic (loss) income per share is computed by dividing income available to common stockholders by the weighted average number of common shares outstanding at the end of the period.

Diluted earnings per share is computed using the weighted-average number of common shares and dilutive potential common shares outstanding during the period. Dilutive potential common shares primarily consist of stock options, convertible notes and warrants to purchase common shares (See "CAPITALIZATION").

# NOTE 3. COMPOSITION OF CERTAIN BALANCE SHEET CAPTIONS

Inventories at December 31, 2008, consist of the following:

Property and equipment, net, consists of the following at December 31, 2008:

Furniture and equipment Leasehold improvements Tooling and molds	,	43,642 0 64,785 
Less accumulated depreciation and amortization	\$10	08,209
	\$ ==	218 =====

Accounts payable and accrued expenses consist of the following at December 31, 2008:

Accounts payable	\$441,653
Accrued vacation	18,409
Accrued compensation	10,743
Sales and use tax	233
Sub-Lease Security Deposit	7,500
Accrued professional fees	0
Customer deposits	0
Commissions Payable	0
Accrued payroll tax	0
Total accounts payable and accrued expenses	\$478,538
	======

# NOTE 4. SENIOR CONVERTIBLE SECURED NOTES DUE TO OFFICER

At December 31, 2008, the Company had sold an aggregate of \$900,000 of 6% senior convertible secured notes (the "Convertible Notes") to its Chief Executive Officer and \$50,000 of Convertible Notes to each of two directors. The Convertible Notes are convertible, including accrued interest thereon, into common stock, at \$0.50 per Share (the "Conversion Price").

### **NOTE 5. INCOME TAXES**

10 60 L

At December 31, 2008, the Company had a net operating loss carry-forward ("NOL") of \$7,301,815. As a result, no federal income tax is expected to be due for the year ended December 31, 2009.

### NOTE 6. COMMITMENTS AND CONTINGENCIES

### **Lease Commitments**

The Company has a non-cancelable operating lease for its office and factory in Irvine, CA, at a rental of \$ 24,049 per month which expires in January 2010, part of which is subleased to an unaffiliated party (See "Properties").

### Product liability

The Company is subject to various claims and actions which arise in the ordinary course of business. The litigation process is inherently uncertain, and it is possible that the resolution of any of the Company's existing and future litigation may adversely affect the Company. Management is not aware of any matters which are not reflected in the financial statements that may have material impact on the Company's financial position, results of operations or cash flows.

### Guarantees and Indemnities

The Company has made certain indemnities and guarantees, under which it may be required to make payments to a guaranteed or indemnified party. The Company is not in default or in breach of any of such indemnities or guarantees. The Company indemnifies its directors, officers, employees and agents to the maximum extent permitted under the laws of the State of Nevada. In connection with its facility leases, the Company has indemnified its lessors for certain claims arising from the use of the facilities. The duration of the guarantees and indemnities varies, and in many cases is indefinite. These guarantees and indemnities do not provide for any limitation of the maximum potential future payments the Company could be obligated to make. Historically, the Company has not been obligated to make any payments for these obligations and no liabilities have been recorded for these indemnities and guarantees in the accompanying consolidated balance sheet.

# Stock Options

The Company has adopted stock option plans that authorize the granting of options to key officers, employees, directors, and consultants to purchase unissued common stock subject to certain conditions, such as continued employment. Options are generally granted at the last sales price of shares to unaffiliated parties or fair market value of the Company's common stock at the date of

grant, become exercisable over a period of five years from the date of grant, and generally expire in six or ten years specific to their respective plan. Forfeitures of stock options are returned to the Company and become available for grant under the respective plan (See "Stock Options").

At December 31, 2008, the Company had outstanding stock options to purchase a total of 1,088,000 Shares at prices ranging from \$2.35 to \$2.50 per Share (average exercise price \$2.48 per Share), of which options to purchase 603,000 Shares were then exercisable.

### NOTE 8. EMPLOYEE BENEFIT PLAN

The Company presently has no retirement plan for its officers or employees.

### **NOTE 9. SEGMENT INFORMATION:**

The Company's revenues are derived from the sales of its product on a worldwide basis originating from the United States. Although discrete components that earn revenues and incur expenses exist, significant expenses such as research and development and corporate administration are not incurred by nor allocated to these operating units but rather are employed by the entire enterprise. Additionally, the chief operating decision maker evaluates resource allocation not on a product or geographic basis, but rather on an enterprise-wide basis. Therefore, the Company has concluded that it contains only one reportable segment, which is the Company's medical device business.

All the Company's long-lived assets were located in the United States at December 31, 2008.

### NOTE 10. RELATED PARTY TRANSACTIONS

See "Related Party Transactions".

### NOTE 11. SUBSEQUENT EVENTS

The Company had no material subsequent events since December 31, 2008, except for (a) the sale of \$550,000 of Convertible Notes in March 2009 to Thomas R. Ulie, one of the Company's Directors, (b) our shareholders approved the reservation of an additional 1,000,000 shares for granting of stock options to our officers, directors, employees and consultants, and (c) the Company's anticipating a reduction in sales and a delay in orders if the current worldwide recession and credit shortage becomes more severe or is prolonged, causing distributors, physicians, group practices, clinics and hospitals to conserve cash and causing patients to delay healthcare expenditures.

# MANUALLY SIGNED COPY OF SIGNATURE PAGE ATTACHED

### PART III

# INFORMATION NOT REQUIRED IN THE OFFERING CIRCULAR

### Item 24. Indemnification of Directors and Officers

Section 78.751 of the Nevada Revised Statutes, as amended, authorizes us to indemnify any of our directors or officers under certain prescribed circumstances and, subject to certain limitations, against certain costs and expenses, including attorneys' fees and costs actually and reasonably incurred in connection with any action, suit or proceeding, whether civil, criminal, administrative or investigative, to which the director or officer is a party by reason of being one of our directors or officers, if it is determined that the director or officer acted in accordance with the applicable standard of conduct set forth in those statutory provisions. Article 12 of our Certificate of Incorporation contains provisions relating to the indemnification of our directors and officers to the fullest extent permitted by Nevada law.

We may also purchase and maintain insurance for the benefit of any director or officer that may cover claims for which we could not indemnify such person.

# Item 25. Other Expenses of Issuance and Distribution

In addition to commissions we may be obligated to pay to member firms of the NASD on sales of the 1,000,000 Shares being offered to the public by them, if any, the following statement sets forth the estimated expenses of this Offering as described in the Offering Circular.

Securities and Exchange Commission fee	\$ 0
Legal fees and expenses	35,000
Blue Sky fees and expenses	20,000
Printing and mailing costs	15,000
Miscellaneous	30,000
TOTAL	\$ 100,000

# Item 26. Recent Sales of Unregistered Securities

- (a) The Company sold an aggregate of \$900,000 of 6% Senior, Secured Convertible Notes (the "Notes") to its Chairman and CEO and \$50,000 of such Notes to each of two of our Directors in private transactions from June 1, 2005 through December 31, 2008. The Company sold an additional \$550,000 of Notes in March 2009 to one of the Company's Directors in private transactions. The principal and any accrued interest on the Notes are convertible into Stares at a conversion price of \$0.50 per share.
- (b) At various times from April 2006 through December 31, 2008, the Company issued 720,000 Shares to its Chairman and CEO in lieu of cash compensation for his serving as its Chairman and CEO from January 1, 2006 through December 31, 2008.

With respect to the transactions described in (a) and (b) above, we relied upon the exemption from registration provided by Section 4(2) of the Securities Act of 1933, as amended, as transactions not involving a public offering.

### Item 27. Exhibits

The following exhibits are filed with this Registration Statement:

THE IONOW	ing exhibits are filed with the region and reaction.	Page No.
2.1	Underwriting Agreement – None.	
2.2	Articles of Incorporation, Amendments and By-Laws	III-5
2.4	Subscription Agreement	III-50
11.0	Opinion of Counsel	III-57
15.0	Copies of Publications cited in the footnotes to "Results	
	of Clinical Studies" under "BUSINESS", Page 22 of Part II.	III-59

# Item 28. <u>Undertakings</u>

The undersigned registrant hereby undertakes:

- (1) To file, during any period in which offers or sales are being made, a postqualification amendment to this registration statement to include any material information with respect to any sale of Shares not previously disclosed in the registration statement or any material change to the information in the registration statement.
- (2) That, for the purpose of determining any liability under the Securities Act of 1933, each such post-qualification amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.
- (3) To remove from registration by means of a post-qualification amendment any of the securities being registered which remain unsold at the termination of the offering.

- (4) The undersigned registrant hereby undertakes that, for the purpose of determining any liability under the Securities Act of 1933, each future filing of any annual report pursuant to section 13 (a) or section 15 (d) of the Securities Exchange Act of 1934 (and, where applicable, each filing of any employee benefit plan's annual report pursuant to section 15(d) of the Securities Act of 1934) that may be incorporated by reference in the registration statement shall be deemed to be a new registration statement relating to the securities being offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.
- (5) Insofar as indemnification against liabilities arising under the Securities Act of 1933 may be permitted to directors, officers and controlling persons of the Registrant pursuant to the foregoing provisions or otherwise, the Registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the Registrant of expenses incurred or paid by a director, officer, or controlling person of the Registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the Registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Act and will be governed by the final adjudication of such issue.

### **SIGNATURES**

Pursuant to the requirements of the Securities Act of 1933, the Registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing a Registration Statement on Form 1-A and has duly caused this Registration Statement or Amendment to the Registration Statement on Form 1-A to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Irvine, State of California, on the 30thday of March 2009.

 CARDIOMEDICS, II	2	
Marvin P. Loeb Chairman and Chie		ficer

Pursuant to the requirements of the Securities Act of 1933, this Registration Statement or Amendment to the Registration Statement has been signed below by the following persons in the capacities and on the dates indicated.

Signature	Title	Date 
Matrin P. Loeb	Chairman, Chief Executive Officer and Director	March 30, 2009
John McCallum	President, COO and Director	March 30,2009
Lorrie L. Stratton	Chief Accounting Officer	March 30, 2009
Donald Saher	Director	March::304,2009
Thomas R. Ulie	Director	March 30, 2009
Glenn D. Yeik	Director	March 30, 2009

### **SIGNATURES**

Pursuant to the requirements of the Securities Act of 1933, the Registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing a Registration Statement on Form 1-A and has duly caused this Registration Statement or Amendment to the Registration Statement on Form 1-A to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Irvine, State of California, on the day of, 2009.		
CARDIOMEDICS, INC.		
Marvin P. Loeb Chairman and Chief Executive Officer		
Pursuant to the requirements Amendment to the Registration State capacities and on the dates indicated.	s of the Securities Act of 1933, this ement has been signed below by the	Registration Statement or e following persons in the
Signature	Title	Date
Marvin P. Loeb	Chairman, Chief Executive Officer and Director	2009
John McCallum	President, COO and Director	2009
Lorrie L. Stratton	Chief Accounting Officer	2009
Donald Barker	Director	2009
Thomas R. Ulie	Director	March 30, 2009
Glenn D. Yeik	Director	2009

# CARDIOMEDICS, INC. Form 1-A Registration Statement

**EXHIBIT 2.2** 

ARTICLES OF INCORPORATION, AMENDMENTS & BY-LAWS

PILING FEE: \$250.00 BY: C T CURPURATION SYSTEM ONE EAST FIRST ST. #1600 RENO, NV 80501

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### ARTICLES OF INCORPORATION

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OF

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CARDIONEDICS, INC.

FIRST. The name of the corporation is CARDIOMEDICS, INC.

SECOND. Its principal office in the State of Nevada is located at One East First Street, Reno, Washoe County, Nevada 89501. The name and address of its resident agent is The Corporation Trust Company of Nevada, One East First Street, Reno, Nevada 89501.

THIRD. The nature of the business, or objects or purposes to be transacted, promoted or carried on are:

To engage in any lawful activity and to manufacture, purchase or otherwise acquire, invest in, own, mortgage, pledge, sell, assign and transfer or otherwise dispose of, trade, deal in and deal with goods, wares and merchandise and personal property of every class and description.

To perform research and development services and to manufacture and market health care devices, products and services.

To hole, purchase and convey real and personal estate and to mortgage or lease any such real and personal estate with its franchises and to take the same by devise or bequest.

To acquire, and pay for in cash, stock or bonds of this corporation or otherwise, the goodwill, rights, assets and property, and to undertake or assume the whole or any part of the obligations or liabilities of any person, firm, association or corporation.

To acquire, hold, use, sell, assign, lease, grant licenses in respect of, mortgage, or otherwise dispose of letters patent of the United States or any foreign country, patent rights, licenses and privileges, inventions, improvements and processes, copyrights, trademarks and trade names, relating to or useful in connection with any business of this corporation.

To quarantee, purchase, hold, sell, assign, transfer, mortgage, pledge or otherwise dispose of the shares of the capital
stock of or any bonds, securities or evidences of the indebtedness created by any other corporation or corporations of this
state, or any other state or government, and, while owner of such
stock, bonds, securities or evidence of indebtedness, to exercise
all the rights, powers and privileges of ownership, including the
right to vote, if any.

To borrow money and contract debts when necessary for the transaction of its business, or for the exercise of its corporate rights, privileges or franchises, or for any other lawful purpose of its incorporation; to issue bonds, promissory notes, bills of exchange, debantures, and other obligations and evidences of indebtedness, payable at specified time or times, or payable upon the happening of a specified event or events, whether secured by mortgage, pledge or otherwise, or unsecured, for money borrowed, or in payment for property purchased, or acquired, or for any other lawful objects.

To purchase, hold, sell and transfer shares of its own capital stock, and use therefor its capital, capital surplus,

surplus, or other property or funds; provided it shall not use its funds or property for the purchase of its own shares of capital stock when such use would cause any impairment of its capital; and provided further, that shares of its own capital stock belonging to it shall not be voted upon, directly or indirectly, nor counted as outstanding, for the purpose of computing any stockholders, quorum or vote.

To conduct business, have one or more offices, and hold, purchase, mortgage and convey real and personal property in this state, and in any of the several states, territories, possessions and dependencies of the United States, the District of Columbia, and in any foreign countries.

To do all and everything necessary and proper for the accomplishment of the objects hereinbefore enumerated or necessary or incidental to the protection and benefit of the corporation, and, in general, to carry on any lawful business necessary or incidental to the attainment of the objects of the corporation, whether or not such business is similar in nature to the objects hereinbefore set forth.

The objects and purposes specified in the foregoing clauses shall, except where otherwise expressed, be in nowise limited or restricted by reference to, or inference from, the terms of any other clause in these articles of incorporation, but the objects and purposes specified in each of the foregoing clauses of this article shall be regarded as independent objects and purposes.

FOURTH. The aggregate number of shares which the corporation is authorized to issue is 24,000,000 with said shares being divided into two classes. The designation of each class, the number of shares of each class, and the par value, if any, of the shares of each class, or a statement that the shares of any class are without par value, are as follows:

Class	Series (if any)	Number of Shares	par value per share or statement that shares are without par value
Common	Class B	20,000,000 4,000,000	\$.01 \$.01

The preference, qualifications, limitations, restrictions, and the special or relative rights in respect of the shares of each class are as follows:

The Common Stock and the Class B Common Stock of the Company will be, when issued, fully paid and non-assessable.

Holders of the Common Stock and Class B Common Stock shall be entitled equally to their pro rata share of such dividends and distributions as may be declared from time to time by the Board of Directors.

The Class B Common Stock is convertible at any time into Common Stock on a share-for-share basis.

The holders of the Class B Common Stock will not share in the assets of the Company in the event of liquidation or dissolution until the holders of the Common Stock have received \$.50 per share, after which holders of the Class B stock will receive \$.50

per share. Thereafter, both classes will share equally in any remaining assets. Shareholders will have no preemptive rights to subscribe for any securities of the Company.

Holders of the Common Stock and the Class B Common Stock will each be entitled to one vote per share. The holders of the Class B Common Stock will be entitled to elect at any time a majority of the Company's Board of Directors, but will not be entitled to cumulative voting. Holders of the Common Stock will be entitled to cumulate their votes in the election of the remaining directors.

known as directors, and the number of directors may from time to time be increased or decreased in such manner as shall be provided by the by-laws of this corporation, provided that the number of directors shall not be reduced to less than three (3), except that in cases where all the shares of the corporation are owned beneficially and of record by either one or two stockholders, the number of directors may be less than three (3) but not less than the number of stockholders.

The names and post-office addresses of the first board of directors, which shall be four (4) in number, are as follows:

PARE	Post-Office Address		
Harvin Loab	1815 East Carnegie Avenue Santa Ana, California 92705		
Bruce N. Barron	2250 East Devon Avenue Des Plaines, Illinois 60018		
Russell C. Chambers, H.D.	1815 Eist Carnogie Avenue Santa Ana, California 92705		

- 6 -

Donald Baker

Baker & McKenzia 3200 Prudential Plaza Chicago, Illinois 60601

SIXTH. The capital stock, after the amount of the subscription price or par value has been paid in, shall not be subject to assessment to pay the debts of the corporation.

SEVENTH. The name and post-office address of the incorporator signing the articles of incorporation is:

Name

Post-Office Address

Mary K. Bentley

Baker & McKenzie 2900 Prudential Plaza Chicago, Illinois 60601

EIGHTH. The corporation is to have perpetual existence.

NINTH. In furtherance, and not in limitation of the powers conferred by statute, the board of directors is expressly authorized:

Subject to the by-laws, if any, adopted by the stockholders, to make, alter or amend the by-laws of the corporation.

To fix the amount to be reserved as working capital over and above its capital stock paid in, to authorize and cause to be executed mortgages and liens upon the real and personal property of this corporation.

By resolution passed by a majority of the whole board, to designate one (1) or more committees, each committee to consist of one (1) or more of the directors of the corporation, which, to the extent provided in the resolution or in the by-laws of the corporation, shall have and may exercise the powers of the board

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of directors in the management of the business and affairs of the corporation, and may authorize the seal of the corporation to be affixed to all papers which may require '. Such committee or committees shall have such name or names as may be stated in the by-laws of the corporation or as may be determined from time to time by resolution adopted by the board of directors.

when and as authorized by the affirmative vote of stockholders holding stock entitling them to exercise at least a
majority of the voting power given at a stockholders' meeting
called for that purpose, or when authorized by the written consent of the holders of at least a majority of the voting stock
issued and outstanding, the board of directors shall have power
and authority at any meeting to sell, lease or exchange all of
the property and assets of the corporation, including its good
will and its corporate franchises, upon such terms and conditions
as its board of directors deem expedient and for the best interests of the corporation.

TENTH. Meetings of stockholders may be held outside the State of Nevada, if the by-laws so provide. The books of the corporation may be kept (subject to any provision contained in the statutes) outside the State of Nevada at such place or places as may be designated from time to time by the board of directors or in the by-laws of the corporation.

ELEVENTH. This corporation reserves the right to amend, alter, change or repeal any provision contained in the articles of incorporation, in the manner now or hereafter prescribed by

statute, or by the articles of incorporation, and all rights conferred upon stockholders herein are granted subject to this reservation.

I, THE UNDERSIGNED, being the incorporator hereinbefore named, for the purpose of forming a corporation pursuant to the General Corporation Law of the State of Nevada, do make and file these articles of incorporation, hereby declaring and certifying that the facts herein stated are true, and accordingly have hereunto set my hands the 22nd day of August, 1986.

Mary K. Bentley

STATE OF ILLINOIS COUNTY OF COOK

On this 22nd day of August, 1986, before me, a Notary Public, personally appeared Mary K. Bentley, who acknowledged that she executed the above instrument.

Notary Public

FILED

IN THE OFFICE OF THE SECTETARY OF STATE OF NEVADA

(53792)

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CERTIFICATE OF AMENDMENT

OF

AL. ICLES OF INCORPOSATION

Cardiomedics, Inc., a corporation organized under the laws of the State of Nevada, by its president and secretary does hereby certify:

1. That the board of directors of said corporation by unanimous written consent dated as of September 24, 1987 passed resolutions declaring that the following changes and amendments in the articles of incorporation are advisably.

RESOLVED, that Article Four of the Articles of Incorporation of the Corporation be amended by replacing the first paragraph of said Article Four with the following:

Fourth. The aggregate number of shares which the corporation is authorized to issue is 23,000,000 with said shares being divided into two classes. The designation of each class, the number of shares of each class, and the par value, if any, of the shares of each class, or a statement that the shares of any class are without per value, are as follows:

			statement that shares are
Class	Secies (if any)	Number of Shares	value
Common	Class B	20,000,000 3,000,000	\$.01 \$.01

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RESOLVED, that the Board of Directors recommends to the stockholders that the Articles of Incorporation of the Corporation be amended to add a new article as follows:

TWELFTH. The By-laws of the corporation shall provide for the indemnification of the corporation's directors, officers, employees and agents for expenses incurred in connection with the defense of actions, suits or proceedings to the fullest extent permitted by Nevada law.

RESOLVED, that the Board of Directors recommends to the stochholders that the Articles of Incorporation be amended to add a new article as follows:

THIRTEENTH. No director or officer of the Corporation shall be liable to the Corporation -t to the stockholders for damages for any breach of fluuciary duty; provided however, that a director or officer shall be liable for damages which result from any of the following:

- (a) Acts or omissions which involve intentional misconduct, fraud or a knowing violation of law;
- (b) The wilfull or grossly negligent payment of any improper dividend or distribution; or
- (c) Acts or omissions which occurred prior to March 18, 1987.
- 2. That the number of shares of the corporation outstanding and entitled to vote on an amendment to the articles of incorporation is 5,200,000 of which 2,400,000 shares are outstanding shares of Common Stock and of which 2,800,000 shares are outstanding shares of Class B Common Stock; that that said changes and amendments have been consented to and authorized by the written consent of stockholders helding at least a majority of each plass of stock outstanding and entitled to vote thereon.

ORIGINAL DOCUMENT INSUFFICIENT QUALITY FOR PROPER REPRODUCTION SECRETARY OF STATE

IN WITHESS MHEREOF; the said Cardiomedics, Inc. has caused this certificate to be signed by its president and its secretary and its corporate seal to be hereto allied this July day of September, 1987.

BY HOWARD R. CUOPS . Prevident

(SEAL)

COUNTY OF So Urgeico

on <u>Not.14,1987</u> personally appeared before me. a Notary Public, Howard K. Cooper, President of Cardiomedics, Inc., who acknowledged that he executed the above instrument.

(Boesey Public)



(SEAL)

ORIGINAL DOCUMENT INSUFFICIENT QUALITY FOR PROPER REPRODUCTION SECRETARY OF STATE

STATE OF Cilifornia ;

on 11 14 till personally appeared before me, a Inc., who acknowledged that she executed the above instrument.

Meri Mincolkapter



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#### CERTIFICATE OF AMENDMENT

OF

#### ARTICLES OF INCORPORATION

CARDIOMEDICS, INC., a corporation organized under the laws of the State of Nevada (the "Corporation"), by its president (or vice-president) and secretary (or assistant secretary) does hereby certify:

- a meeting of the board of directors of said Corporation at a meeting of the board of directors of the Corporation held on December 23, 1991 and by unanimous written consent dated the \_\_\_\_\_ day of \_\_\_\_\_, 1992, unanimously passed resolutions declaring that the changes and amendments in the Articles of Incorporation hereinafter set forth are advisable, and called that action be taken thereon by the stockholders by written consent in lieu of a meeting.
- 2. That thereafter, on the \_\_ day of \_\_\_\_\_\_, 1992, pursuant to such call of the board of directors, the stockholders of record entitled to vote on an amendment to the Articles of Incorporation as provided by law, holding at least a majority of the shares outstanding and entitled to vote thereon, approved and adopted such changes and amendments, being as follows:
- 3. That Article Fourth of the Articles of Incorporation of the Corporation be amended to read as follows:

FOURTH: The aggregate number of shares which the Corporation is authorized to issue is 20,000,000 shares of Common Stock of the

par value of One Cent (\$0.01) each, amounting in the aggregate to Two Hundred Thousand Dollars (\$200,000).

The Common Stock of the Corporation will be, when issued, fully paid and non-assessable.

Holders of the Common Stock shall be entitled to their pro rata share of such dividends and distributions as may be declared from time to time by the Board of Directors.

liquidation, of any event the dissolution or winding up of the affairs of Corporation, whether voluntary involuntary, all assets and funds of the Corporation available for distribution to its shareholders shall be distributed and paid over to the holders of the Common Stock at the rate of fifty cents (\$0.50) per share. Should remain for distribution after the assets aforementioned allocation, the holders of the Common Stock shall share equally in any remaining assets. Shareholders will have no for preemptive rights to subscribe securities of the Company.

Holders of the Common Stock will each be entitled to one vote per share.

4. That the Articles of Incorporation be amended to add new Articles Twelfth and Thirteenth as follows:

TWELFTH: The By-Laws of the Corporation shall provide for the indemnification of the Corporation's directors, officers, employees and agents for expenses incurred in connection with the defense of actions, suits or proceedings to the fullest extent permitted by Nevada law.

THIRTEENTH: No director or officer of the Corporation shall be liable to the Corporation or to the stockholders for damages for any breach of fiduciary duty; provided, however, that a director or officer shall be liable for damages which result from any of the following:

- (a) Acts or omissions which involve intentional misconduct, fraud or a knowing violation of law;
- (b) The wilful or grossly negligent payment of any improper dividend or distribution; or
- (c) Acts or omissions which occurred prior to March 18, 1987.

WE, THE UNDERSIGNED, do make and file these amendments to the Articles of Incorporation, hereby declaring and certifying that the facts herein are true, and accordingly, have hereunto set our hands this \_\_\_ day of \_\_\_\_\_, 1992.

William T. Delilt

Secretary

(015220.1)

State of	) ) SS.:			
County of	)			
On this	day of	, 1992, before me, a		
Notary Public, perso	nally appeared	, and		
, who	severally acknowledge	owledged that they executed the		
above instrument.				
		Notary Public		
		Commission expires:		



Certificate of Amendment (PURSUANT TO NRS 78,585 AND 78,390)

Filed in the office of · en Me

Ross Miller

State of Nevada

Document Number 20090209167-26

Filing Date and Time

03/04/2009 10:02 AM Secretary of State

Entity Number C5967-1986

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Cartificate of Amendment to Articles of Incorporation
For Nevada Profit Corporations (Pursuant to NRS 78,385 and 78,380 - After Issuance of Stock)

1. Name of corporation:

CARDIOMEDICS. INC.

2. The articles have been amended as follows (provide article numbers, if available):

The total number of shares of authorized aspital apole of the Corporation currently assisted of twenty three million (23,000,000) alterne of stock at 9.01 per value. This Corporation stock should be arounded to reflect forty one million (41,000,000) shares of stock at \$.01. The authorized starps shall be divided into two (2) classes of stock, facinting one (1) classes of Preferred Stock, and one (1) class of Common Stock. The number of shares within each class to be authorized will be as follows:

40,000,000 shares of Common Stock at \$.01 per value · 1.000,000 shares of Preferred Stock at \$.01 per value

- The vote by which the stockholders holding shares in the corporation entiting them to exercise at least a majority of the voting power, or such greater proportion of the voting power as may be required in the case of a vote by classes or series, or as may be required by the provisions of the articles of incorporation have voted in favor of the amendment is: 78.31
- Effective date of filing (optional):

Officer Bignetime (Required);

"If any proposed amendment would all Car change any prefere e or any relative or other right glean to any class or acrima of of the holders of shares representing a majority of the voting power of each cities or series affected by the amendment required, of the holders or series affected by the amendment regardless of implications or restrictions on the voting power thereof. ration the vote, in addition to the elfimative vote otherwise required.

IMPORTANT: Fallure to include any of the above information and submit the proper fees may cause this filing to be rejected.

This form must be encompanied by appropriate fees.

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ROSS MILLER
Secretary of State
204 North Carson Street, Ste 1
Carson City, Nevada 89701-4299
(775) 684 5708
Website: secretaryofstate.biz

#### **Certificate of Amendment**

(PURSUANT TO NRS 78.385 AND 78.390)

USE BLACK INK ONLY - DO NOT HIGHLIGHT

ABOVE SPACE IS FOR OFFICE USE ONLY

## Certificate of Amendment to Articles of Incorporation For Nevada Profit Corporations (Pursuant to NRS 78.385 and 78.390 - After Issuance of Stock)

1. Name of corporation:
CARDIOMEDICS, INC.
2. The articles have been amended as follows (provide article numbers, if available):

The total number of shares of authorized capital stock of the Corporation currently consists of twenty three million (23,000,000) shares of stock at \$.01 par value. This Corporation stock should be amended to reflect forty one million (41,000,000) shares of stock at \$.01. The authorized shares shall be divided into two (2) classes of stock, including one (1) classes of Preferred Stock, and one (1) class of Common Stock. The number of shares within each class to be authorized

40,000,000 shares of Common Stock at \$.01 par value 1,000,000 shares of Preferred Stock at \$.01 par value

3. The vote by which the stockholders holding shares in the corporation entitling them to exercise at least a majority of the voting power, or such greater proportion of the voting power as may be required in the case of a vote by classes or series, or as may be required by the provisions of the\* articles of incorporation have voted in favor of the amendment is:

4. Effective date of filing (optional):

(must not be later than 90 days after the certificate is filed)

5. Officer Signature (Required):

will be as follows:

\*If any proposed amendment would alter or change any preference or any relative or other right given to any class or series of outstanding shares, then the amendment must be approved by the vote, in addition to the affirmative vote otherwise required, of the holders of shares representing a majority of the voting power of each class or series affected by the amendment regardless of limitations or restrictions on the voting power thereof.

**IMPORTANT:** Failure to include any of the above information and submit the proper fees may cause this filing to be rejected.

This form must be accompanied by appropriate fees.

Nevada Secretary of State AM 78.385 Amend 2007 Revised on: 01/01/07

#### CERTIFICATE OF AMENDMENT

OF

#### ARTICLES OF INCORPORATION

Cardiomedics, Inc., a corporation organized under the laws of the State of Nevada, by its president and secretary does hereby certify:

1. That the board of directors of said corporation by unanimous written consent dated as of December 12, 2008, passed resolutions declaring that the following changes and amendments in the articles of Incorporation are advisable.

RESOLVED, that Article Four of the Articles of Incorporation of the Corporation be amended by replacing Articles Four in its entirety with the following:

FOURTH. The aggregate number of shares which the corporation is authorized to issue is 41,000,000 with said shares being divided into two classes. The designation of each class, the number of shares of each class, and the par value, if any, of the shares of each class, or a statement that the shares of any class are without par value, are as follows:

<u>Class</u>	Series (if any)	Number of Shares	Par value per share of statement that shares are without par value
Common		40,000,000	\$.01
Preferred		1,000,000	No Par Value

The preference, qualifications, limitations, restrictions, and the special or relative rights in respect of the shares of each class are as follows:

The Common Stock and Preferred Stock of the Corporation will be, when issued, fully paid and non-assessable.

Holders of the Common Stock shall each have one vote per share and shall be entitled equally to their pro rata share of such dividends and distributions as may be declared from time to time by the Board of Directors.

The rights, preferences, qualifications, limitations and restrictions of the Preferred Stock, if any, shall be fixed by the Board of Directors of the Corporation at the time of issuance of each class, if any, of the Preferred Stock.

In the event of liquidation or dissolution of the Corporation, the holders of Common Stock will share equally in any assets of the Corporation, subject to whatever prior rights in liquidation or dissolution, if any, may have been granted to the holders of Preferred Stock by the directors of the Corporation.

Shareholders will have no preemptive rights to subscribe for any securities of the Corporation and will not be entitled to cumulative voting in the election of directors.

2. That the number of shares of the corporation outstanding at the close of business on December 29, 2008, and entitled to vote on an amendment to the articles of incorporation of the corporation was 7,437,980 shares of Common Stock, and said change and amendment has been consented to and authorized by the written consent of stockholders holding at least a majority of the shares of each class of stock of the corporation outstanding and entitled to vote thereon.

IN WITNESS WHEREOF, Cardiomedics, Inc. has caused this certificate to be signed by its president and its secretary and its corporate seal to be hereto affixed this 12 day of february, 2009.



CARDIOMEDICS, INC

John McCallum. President

(SEAL)

STATE OF California

COUNTY OF SUN DIEGO,

On Feb. 23rd , 2009 personally appeared before me, a Notary

Public, John McCallum, President of Cardiomedics, Inc., who acknowledged that he

executed the above instrument.

(Notary Public)

(SEAL)

STATE OF

COUNTY OF

SS:

2009 personally appeared before me, a Notary

Public, Alan E. Loeb, Secretary of Cardiomedics, Inc., who acknowledged that he

executed the above instrument.

(SEAL)



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#### CARDIOMEDICS, INC.

#### BY-LAWS

#### ARTICLE 1

#### OFFICES

Section 1. The registered office of the corporation shall be in the City of Reno, County of Washoe, State of Nevada. The principal office for the transaction of the business of the corporation shall be in the City of Santa Ana, County of Orange, State of California.

Section 2. The Corporation may also have offices at such other places both within and without the State of Nevada as the board of directors may from time to time determine or the business of the corporation may require.

#### ARTICLE II

#### MEETINGS OF STOCKHOLDERS

Section 1. Election of directors shall take place at the annual meeting of stockholders.

Section 2. Annual meetings of stockholders shall be held on the first Tuesday of February if not a legal holiday; and if a legal holiday, then on the next secular day following, at 11:00 A.M. at the principal office of the corporation; or at such other date, time and place as shall be designated from time to time by the board of directors and stated in the notice of the meeting, at which they shall elect a board of directors, and transact such other business as may properly be brought before the meeting.

Section 3. Written notice of the annual meeting stating the place, date and hour of the meeting shall be given to each stock-holder entitled to vote at such meeting not less than ten nor more than sixty days before the date of the meeting.

The officer who has charge of the stock ledger of the corporation shall prepare and make, at least ten days before every meeting of stockholders, a complete list of the stockholders entitled to vote at the meeting, arranged in alphabetical order, and showing the address of each stockholder and the number of shares registered in the name of each stockholder. Such list shall be open to the examination of any person who has been a stockholder of record for at least six (6) months prior to the demand for such inspection or who holds at least five per cent (5%) of all outstanding shares of the corporation, for any purpose germane to the meeting, during ordinary business hours, for a period of at least ten days prior to the meeting, either at a place within the city where the meeting is to be held, which place shall be specified in the notice of the meeting, or, if not so specified, at the place where the meeting is to be held. list shall also be produced and kept at the time and place of the meeting during the whole time thereof, and may be inspected by any stockholder who is present.

Section 5. Special meetings of the stockholders, for any purpose or purposes, unless otherwise prescribed by statute or by the certificate of incorporation, may be called by the chairman and shall be promptly called by the chairman, president or secre-

tary at the request in writing of a majority of the board of directors or at the request in writing of stockholders owning at least one-fifth of the shares of the corporation issued and outstanding and entitled to vote. Such request shall state the purpose or purposes of the proposed meeting.

Section 6. Written notice of a special meeting stating the place, date and hour of the meeting and the purpose or purposes for which the meeting is called, shall be given not less than ten nor more than sixty days before the date of the meeting, to each stockholder entitled to vote at such meeting.

Section 7. Business transacted at any special meeting of stockholders shall be limited to the purposes stated in the notice.

Section 8. Holders of one-third of the shares issued and outstanding and entitled to vote thereat, present in person or represented by proxy, shall constitute a quorum at all meetings of the stockholders for the transaction of business except as otherwise provided by statute or by the certificate of incorporation. If, however, such quorum shall not be present or represented at any meeting of the stockholders, the stockholders entitled to vote thereat, present in person or represented by proxy, shall have power to adjourn the meeting from time to time, without notice other than announcement at the meeting, until a quorum shall be present or represented. At such adjourned meeting at which a quorum shall be present or represented any business may be transacted which might have been transacted at the

meeting as originally notified. If the adjournment is for more than thirty days, or if after the adjournment a new record date is fixed for the adjournment meeting, a notice of the adjourned meeting shall be given to each stockholder of record entitled to vote at the meeting.

Section 9. When a quorum is present at any meeting, the vote of the holders of a majority of the shares having voting power present in person or represented by proxy shall decide any question brought before such meeting, unless the question is one upon which, by express provision of any statute or of the certificate of incorporation or these by-laws, a different vote is required, in which case such express provision shall govern and control the decision of such question.

Section 10. Each stockholder shall at every meeting of the stockholders be entitled to one vote in person or by proxy for each share of the corporation having voting power held by such stockholder, but no proxy shall be valid after the expiration of six (6) months from the date of its execution, unless coupled with an interest, or unless the person executing it specifies therein that the proxy is irrevocable and the length of time for which it is to continue in force, which in no case shall exceed seven (7) years from the date of its execution; provided that in the election of directors, each stockholder holding shares of Class B Common Stock of the corporation shall be entitled to one vote in person or by proxy for each such share he holds for the election of the majority of the Board of Directors of the corporation o

poration and each shareholder holding shares of Common Stock of the Corporation shall be entitled to one vote in person or by proxy for each such share he holds for the election of the remaining members of the Board of Directors of the corporation. Both the Class B Common Stock and the Common Stock shall have non-cumulative voting rights.

Section 11. Any action, except the election of directors, required to be taken at any annual or special meeting of stockholders of the corporation, or any action which may be taken at any annual or special meeting of such stockholders, may be taken without a meeting, without prior notice and without a vote, if a consent in writing, setting forth the action so taken, shall be signed by the holders of outstanding shares having not less than the minimum number of votes that would be necessary to authorize or take such action at a meeting at which all shares entitled to vote thereon were present and voted, except as may be otherwise specifically provided by statute or by the certificate of incorporation. Prompt notice of the taking of the corporate action without a meeting by less than unanimous written consent shall be given to those stockholders who have not consented in writing.

#### ARTICLE III

#### DIRECTORS

Section 1. The number of directors which shall constitute the whole board shall be three. The directors shall be elected at the annual meeting of the stockholders, except as provided in

Section 2 of this Article, and each director elected shall hold office until his successor is elected and qualified. Directors need not be stockholders.

Vacancies and newly created directorships re-Section 2. sulting from any increase in the authorized number of directors may be filled by a majority of the directors then in office, though less than a quorum, or by a sole remaining director, and the directors so chosen shall hold office until the next annual election and until their successors are duly elected and shall qualify, unless sooner displaced. If there are no directors in office, then an election of directors may be held in the manner provided by statute. If, at the time of filling any vacancy or any newly created directorship, the directors then in office shall constitute less than a majority of the whole board (as constituted immediately prior to any such increase), a court of proper jurisdiction may, upon application of any stockholder or stockholders holding at least ten percent of the total number of the shares at the time outstanding having the right to vote for such directors, summarily order an election to be held to fill any such vacancies or newly created directorships, or to replace the directors chosen by the directors then in office.

Section 3. Any director, whether elected by the stockholder or appointed by the directors, may be removed from office by the vote or written consent of stockholders representing two-thirds of the issued and outstanding stock entitled to voting power.

by its board of directors which may exercise all such powers of the corporation and do all such lawful acts and things as are not by statute or by the certificate of incorporation or by these bylaws directed or required to be exercised or done by the stock-holders.

### MEETINGS OF THE BOARD OF DIRECTORS

Section 5. The board of directors of the corporation may hold meetings, both regular and special, either within or without the State of Nevada.

Section 6. The first meeting of each newly elected board of directors shall be held immediately after the annual meeting of stockholders and no notice of such meeting, other than this bylaw, shall be necessary to the newly elected directors in order legally to constitute the meeting, provided a quorum shall be present. In the event such meeting is not so held, the meeting may be held at such time and place as shall be specified in a notice given as hereinafter provided for special meetings of the board of directors, or as shall be specified in a written waiver signed by all of the directors.

Section 7. Regular meetings of the board of directors may be held without notice at such time and at such place as shall from time to time be determined by the board.

Section 8. Special meetings of the board may be called by the chairman on five days' notice to each director, either personally or by mail or by telegram; and special meetings shall be

promptly called by the chairman, the president or the secretary in like manner and on like notice on the written request of two directors or stockholders owning at least one-fifth of the shares of the corporation issued and outstanding and entitled to vote.

Section 9. At all meetings of the board, a majority of directors then in office shall constitute a quorum for the transaction of business and the act of a majority of the directors, except as may be otherwise specifically provided by statute or by the certificate of incorporation. If a quorum shall not be present at any meeting of the board of directors, the directors present thereat may adjourn the meeting from time to time, without notice other than announcement at the meeting, until a quorum shall be present.

Section 10. Unless otherwise restricted by the certificate of incorporation or these by-laws, any action required or permitted to be taken at any meeting of the board of directors or of any committee thereof may be taken without a meeting, if all members of the board or committee, as the case may be, consent thereto in writing, and the writing or writings are filed with the minutes of proceedings of the board or committee.

Section 11. Unless otherwise restricted by statute, the certificate of incorporation or these by-laws, members of the board of directors, or any committee designated by the board of directors, may participate in a meeting of the board of directors, or any committee, by means of conference telephone or similar communications equipment by means of which all persons

participating in the meeting can hear each other, and such participation in a meeting shall constitute presence in person at the meeting.

#### COMMITTEE OF DIRECTORS

Section 12. Each committee shall fix its own rules of procedure and shall keep regular minutes of its meetings and report the same to the board of directors when required.

#### COMPENSATION OF DIRECTORS

Section 13. The board of directors shall have the authority to fix the compensation of directors. The directors may be paid their expenses, if any, of attendance at each meeting of the board of directors and may be paid a fixed sum for attendance at each meeting of the board of directors or a stated salary as director. No such payment shall preclude any director from serving the corporation in any other capacity and receiving compensation thereof. Members of special or standing committees may be allowed like compensation for attending committee meetings.

#### ARTICLE IV

#### NOTICES

Section 1. Whenever, under the provisions of the statutes or of the certificate of incorporation or of these by-laws, notice is required to be given to any director or stockholder, it shall not be construed to mean personal notice, but such notice may be given in writing, by mail, addressed to such director or

stockholder, at his address as it appears on the records of the corporation, with postage thereon prepaid, and such notice shall be deemed to be given at the time when the same shall be deposited in the United States mail. Notice to directors may also be given by telegram.

Section 2. Whenever any notice is required to be given under the provisions of the statutes or of the certificate of incorporation or of these by-laws, a waiver thereof in writing, signed by the person or persons entitled to said notice, whether before or after the time stated therein, shall be deemed equivalent thereto.

#### ARTICLE V

#### OFFICERS

Section 1. The officers of the corporation shall be chosen by a board of directors and shall be a chairman, a vice chairman, a president, a secretary and a treasurer. The board of directors may also choose one or more vice presidents, and one or more assistant secretaries and assistant treasurers. With the exception of the office of president, any number of offices may be held by the same person, unless the certificate of incorporation or these by-laws otherwise provide.

Section 2. The board of directors at its first meeting after each annual meeting of stockholders shall choose a chairman, a vice chairman, a president, a secretary, and a treasurer.

Section 3. The board of directors may appoint such other officers and agents as it shall deem necessary who shall hold their offices for such terms and shall exercise such powers and perform such duties as shall be determined from time to time by the board.

Section 4. The salaries of all officers and agents of the corporation shall be fixed by the board of directors.

Section 5. The officers of the corporation shall hold office until their successors are chosen and qualify. Any officer elected or appointed by the board of directors may be removed at any time by the affirmative vote of a majority of the board of directors. Any vacancy occurring in any office of the corporation shall be filled by the board of directors.

#### THE CHAIRMAN, THE VICE CHAIRMAN AND THE PRESIDENT

Section 6. The chairman shall be the chief policy and financial officer of the corporation, shall preside at all meetings of the stockholders and the board of directors and shall see that all orders and resolutions of the board of directors are carried into effect. In the absence of the vice chairman, or in the event of his inability to act, the chairman shall perform the duties of the vice chairman.

The vice chairman shall review, advise and consult with the officers of the corporation with respect to the day-to-day business operations of the corporation. In the absence of the chairman or the president, or in the event of the inability of either

of the same to act, the vice chairman shall perform the duties of either or both of the same.

Section 7. The president shall be the chief executive officer of the corporation and shall be responsible for the day-to-day business operations of the corporation. If the chairman and the vice chairman are absent, or if the chairman requests him to do so in writing, the president shall preside at meetings of the stockholders and the board of directors.

Section 8. Any of the chairman, the vice chairman and the president shall be authorized to execute bonds, mortgages and other contracts requiring a seal, under the seal of the corporation, except where required or permitted by law to be otherwise signed and executed and except where the signing and execution thereof shall be expressly delegated by the board of directors to some other officer or agent of the corporation.

#### THE VICE PRESIDENT

Section 9. In the absence of the president or in the event of his inability or refusal to act, the vice president (or in the event there be more than one vice president, the vice presidents in the order designated, or in the absence of any designation, then in the order of their election) shall perform the duties of the president, and when so acting, shall have all the powers of and be subject to all the restrictions upon the president. The vice presidents shall perform such other duties and have such other powers as the board of directors may from time to time prescribe.

### THE SECRETARY AND ASSISTANT SECRETARIES

The secretary shall attend all meetings of the Section 10. board of directors and all meetings of the stockholders and record all the proceedings of the meetings of the corporation and the board of directors in a book to be kept for that purpose and shall perform like duties for the standing committees when required. He shall give, or cause to be given, notice of all meetings of stockholders and special meetings of the board of directors, and shall perform such other duties as may be prescribed by the board of directors or president, under whose supervision he He shall have custody of the corporate seal of the corporation and he, or an assistant secretary, shall have authority to affix the same to any instrument requiring it and when so affixed, it may be attested by his signature or by the signature of such assistant secretary. The board of directors may give general authority to any other officer to affix the seal of the corporation and to attest the affixing by his signature.

Section 11. The assistant secretary, or if there be more than one, the assistant secretaries in the order determined by the board of directors (or if there be no such determination, then in the order of their election), shall, in the absence of the secretary or in the event of his inability or refusal to act, perform the duties and exercise the powers of the secretary and shall perform such other duties and have such other powers as the board of directors may from time to time prescribe.

## THE TREASURER AND ASSISTANT TREASURERS

Section 12. The treasurer shall have the custody of the corporation funds and securities and shall keep full and accurate accounts of receipts and disbursements in books belonging to the corporation and shall deposit all moneys and other moneys and other valuable effects in the name and to the credit of the corporation in such depositories as may be designated by the board of directors.

Section 13. He shall disburse the funds of the corporation as may be ordered by the board of directors, taking proper vouchers for such disbursements, and shall render to the president and the board of directors, at its regular meetings, or when the board of directors so requires, an account of all of his transactions as treasurer of the financial condition of the corporation.

Section 14. If required by the board of directors, he shall give the corporation a bond (which shall be renewed every six years) in such sum and with such surety or sureties as shall be satisfactory to the board of directors for the faithful performance of the duties of his office and for the restoration to the corporation, in case of his death, resignation, retirement or removal from office, of all books, papers, vouchers, money and other property of whatever kind in his possession or under his control belonging to the corporation.

Section 15. The assistant treasurer, or if there shall be more than one, the assistant treasurers in the order determined

by the board of directors (or if there be no such determination, then in the order of their election), shall in the absence of the treasurer or in the event of his inability or refusal to act, perform the duties and exercise the powers of the treasurer and shall perform such other duties and have such other powers as the board of directors may from time to time prescribe.

#### ARTICLE VI

#### CERTIFICATES OF SHARES

Section 1. Every holder of shares in the corporation shall be entitled to have a certificate signed by, or in the name of the corporation by, the chairman or the president and either the treasurer or an assistant treasurer or the secretary or an assistant secretary of the corporation, certifying that the corporation is organized under the laws of the State of Nevada, the name of the person to whom the certificate is issued, the number and class of shares which the certificate represents, and the par value of the shares so represented.

more than one class of shares or more than one series of any class, the powers, designations, preferences and relative, participating, optional or other special rights of each class of shares or series thereof and the qualifications, limitations or restrictions of such preferences and/or rights shall be set forth in full or summarized on the face or back of the certificate which the corporation shall issue to represent such class or

series of shares, provided that in lieu of the foregoing requirements, there may be set forth in the face or back of the certificate which the corporation shall issue to represent such class or series of shares, a statement that the corporation will furnish without charge to each stockholder who so requests the powers, designations, preferences and relative, participating, optional or other special rights of each class of shares or series thereof and the qualifications, limitations or restrictions of such preferences and/or rights.

Section 3. Where a certificate is countersigned (1) by a transfer agent other than the corporation or its employee, or (2) by a registrar other than the corporation or its employee, any other signature on the certificate may be facsimile. In case any officer, transfer agent or registrar who has signed or whose facsimile signature has been placed upon a certificate shall have ceased to be such officer, transfer agent or registrar before such certificate is issued, it may be issued by the corporation with the same effect as if he were such officer, transfer agent or registrar at the date of issue.

#### LOST CERTIFICATES

Section 4. The board of directors may direct a new certificate or certificates to be issued in place of any certificate or certificates theretofore issued by the corporation alleged to have been lost, stolen or destroyed, upon the making of an affidavit of that fact by the person claiming the certificate of shares to be lost, stolen or destroyed. When authorizing such

issue of a new certificate or certificates, the board of directors may, in its discretion and as a condition precedent to the issuance thereof, require the owner of such lost, stolen or destroyed certificate or certificates, or his legal representative, to advertise the same in such manner as it shall require and/or to give the corporation a bond in such sum as it may direct as indemnity against any claim that may be made against the corporation with respect to the certificate alleged to have been lost, stolen or destroyed.

#### TRANSFERS OF SHARES

Section 5. Upon surrender to the corporation or the transfer agent of the corporation of a certificate for shares duly endorsed or accompanied by proper evidence of succession, assignment or authority to transfer, it shall be the duty of the corporation to issue a new certificate to the person entitled thereto, cancel the old certificate and record the transaction upon its books.

#### FIXING RECORD DATE

Section 6. In order that the corporation may determine the stockholders entitled to notice of or to vote at any meeting of stockholders or any adjournment thereof, or to express consent to corporate action in writing without a meeting, or entitled to receive payment of any dividend or other distribution or allotment of any rights, or entitled to exercise any rights in respect of any change, conversion or exchange of shares or for the purpose of any other lawful action, the board of directors may

corporation, subject to the provisions of the certificate of incorporation.

Section 2. Before payment of any dividend, there may be set aside out of any funds of the corporation available for dividends such sum as the directors from time to time, in their absolute discretion, think proper as a reserve or reserves to meet contingencies, or for equalizing dividends, or for repairing or maintaining any property of the corporation, or for such other purpose as the directors shall think conductive to the interest of the corporation, and the directors may modify or abolish any such reserve in the manner in which it was created.

#### ANNUAL STATEMENT

Section 3. The board of directors shall present at each annual meeting, and at any special meeting of the stockholders when called for by vote of the stockholder, a full and clear statement of the business and condition of the corporation.

#### CHECKS

Section 4. All checks or demands for money and notes of the corporation shall be signed by such officers or such other person or persons as the board of directors from time to time designate.

#### FISCAL YEAR

Section 5. The fiscal year of the corporation shall end on September 30, unless otherwise determined by the board of directors.

#### SEAL

Section 6. The corporate seal shall have inscribed thereon the name of the corporation, the year of its organization and the words "Corporate Seal, Illinois". The seal may be used by causing it or a facsimile thereof to be impressed or affixed or reproduced or otherwise.

#### ARTICLE VIII

# INDEMNIFICATION OF DIRECTORS, OFFICERS AND EMPLOYEES

The corporation shall indemnify any person who was or is a party or is threatened to be made a party to any threatened, pending or completed action, suit or proceeding, whether civil, criminal, administrative or investigative, except an action by or in the right of the corporation, by reason of the fact that he is or was a director, officer, employee or agent of the corporation, or is or was serving at the request of the corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise, against expenses, including attorneys' fees, judgments, fines and amounts paid in settlement actually and reasonably incurred by him in connection with such action, suit or proceeding if he acted in good faith and in a manner which he reasonably believed to be in or not opposed to the best interests of the corporation, and, with respect to any criminal action or proceeding, had no reasonable cause to believe his conduct was unlawful. The termination of any action, suit or proceeding by judgment, order, settlement, conviction, or upon a plea of nolo contendere or its equivalent, shall not, of itself, create a presumption that the person did not act in good faith and in a manner which he reasonably believed to be in or not opposed to the best interests of the corporation, and that, with respect to any criminal action or proceeding, he had reasonable cause to believe that his conduct was unlawful.

Section 2. The corporation shall indemnify any person who was or is a party or is threatened to be made a party to any threatened, pending or completed action or suit by or in the right of the corporation to procure a judgment in its favor by reason of the fact that he is or was a director, officer, employee or agent of the corporation, or is or was serving at the request of the corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise against expenses, including attorneys' fees, actually and reasonably incurred by him in connection with the defense or settlement of such action or suit if he acted in good faith and in a manner which he reasonably believed to be in or not opposed to the best interests of the corporation, but no indemnification shall be made in respect of any claim, issue or matters as to which such person has been adjudged to be liable for negligence or misconduct in the performance of his duty to the corporation unless and only to the extent that the court in which such action or suit was brought determines upon application that, despite the adjudication of liability but in view of all the circumstances of the case, such person is fairly and reasonably entitled to indemnify for such expenses as the court deems proper.

Section 3. To the extent that a director, officer, employee or agent of the corporation has been successful on the merits or otherwise in defense of any action, suit or proceeding referred to in subsections 1 and 2, or in defense of any claim, issue or matter therein, he shall be indemnified by the corporation against expenses, including attorneys' fees, actually and reasonably incurred by him in connection with such defense.

Section 4. Any indemnification under subsections 1 and 2, unless ordered by a court, shall be made by the corporation only as authorized in the specific case upon a determination that indemnification of the director, officer, employee or agent is proper in the circumstances because he has met the applicable standard of conduct set forth in the subsections 1 and 2. Such determination shall be made:

(a) By the stockholders;

. \$

- (b) By the board of directors by majority vote of a quorum consisting of directors who were not parties to such act, suit or proceedings;
- (c) If such a quorum of disinterested directors so orders, by independent legal counsel in a written opinion; or

(d) If such a quorum of disinterested directors cannot be obtained, by independent legal counsel in a written opinion.

Section 5. Expenses incurred in defending a civil or criminal action, suit or proceeding shall be paid by the corporation in advance of the final disposition of such action, suit or proceedings as authorized by the board of directors, in the specific case upon receipt of an undertaking by or on behalf of the director, officer, employee or agent to repay such amount unless it is ultimately determined that he is entitled to be indemnified by the corporation as authorized in this section.

Section 6. The indemnification provided by this article:

- a) Does not exclude any other rights to which a person seeking indemnification may be entitled under any by-law, agreement, vote of stockholders or disinterested directors or otherwise, both as to action in his official capacity and as to action in another capacity while holding such office; and
- (b) Shall continue as to a person who has ceased to be a director, officer, employee or agent and shall inure to the benefit of the heirs, executors and administrators of such a person.

Section 7. The corporation may, at the direction of the board of directors, purchase and maintain insurance on behalf of any person who is or was a director, officer, employee or agent of the corporation, or is or was serving at the request of the

corporation as a director, officer, employee or agent of any other corporation, partnership, joint venture, trust or other enterprise against any liability asserted against him and incurred by him in any such capacity, or arising out of his status as such, whether or not the corporation would have the power to indemnify him against such liability under the provisions of this section.

#### ARTICLE IX

#### **AMENDMENTS**

Section 1. These by-laws may be altered, amended or repealed or new by-laws may be adopted by the stockholders or by
the board of directors at any regular meeting of the board of
directors or of the stockholders or at any special meeting of the
board of directors or of the stockholders, if notice of such
alteration, amendment, repeal or adoption or new by-laws be
contained in the notice of such meeting of the stockholders or of
the board of directors.

\* \* \* \* \* \* \*

\_\_\_\_, 1986

## CARDIOMEDICS, INC. Form 1-A Registration Statement

**EXHIBIT 2.4** 

**SUBSCRIPTION AGREEMENT** 

111-50



NAME:	NO. SHARES:	DATE:

# CARDIOMEDICS, INC. SUBSCRIPTION AGREEMENT AND LETTER OF INVESTMENT INTENT

IMPORTANT: <u>PLEASE READ CAREFULLY AND COMPLETE FULLY BEFORE SIGNING;</u> SIGNIFICANT REPRESENTATIONS ARE REQUIRED HEREIN.

John McCallum, President Cardiomedics, Inc. 18872 Bardeen Avenue Irvine, CA 92612

#### Dear Sir:

1.	The Undersigned understands Cardiomedics, Inc. (the "Company") is offering up to 5 million shares of its \$0.01 par value common stock (the "Shares") at a price of \$1.00 per Share pursuant to a Form 1-A Registration Statement under Regulation A (the "Offering"). The Undersigned hereby acknowledges receipt of the Offering Circular, which is Part II of said Registration Statement.
	The Undersigned desires to become a stockholder of the Company and, on this day of, 2009, hereby subscribes, upon the terms and conditions set forth below, for
	the purchase of Shares at a price of \$1.00 per Share for an aggregate purchase price of \$
	A check payable to "CARDIOMEDICS, INC." in full payment of the purchase price for the Shares is attached to this Subscription Agreement. The Undersigned acknowledges this Subscription is contingent upon acceptance in whole or part by the Company in its sole

2. In the event the Undersigned's Subscription for Shares is not accepted in full by the Company, the unaccepted amount of such Subscription shall be promptly refunded to the Undersigned, without interest thereon.

discretion. As used herein, the term "he" shall be construed to mean he, she or it.

3. In consideration of the Undersigned's Subscription Agreement, if accepted by the Company, the Company agrees to issue to the Undersigned, within 60 days after the closing date of the Offering, one-half Class A Warrant for each Share purchased and one-half Class B Warrant for each Share purchased in the Offering. Two (2) Class A Warrants may be exercised to purchase one (1) Share at a price of \$1.50 at any time during a period of six (6) months, commencing twelve (12) months after the closing date of this Offering. Two (2) Class B Warrants may be exercised to purchase one (1) Share at a price of \$2.00 at any time during a period of twelve (12) months, commencing twelve (12) months after the

closing date of this Offering. The Warrants will contain no anti-dilution provisions and are redeemable by the Company on thirty (30) days prior written notice if the Shares trade at a price at least 50% higher than their respective exercise prices for a period of five (5) trading days during their respective exercise periods.

The Class A and B Warrants and the Shares issuable upon exercise of the Class A and B Warrants are not being registered in the Registration Statement of which the Offering Circular is a part. As a result, no market for the Class A or B Warrants is expected to arise. Shares purchased by the exercise of the Class A and B Warrants, if any, may be sold publicly pursuant to Rule 144 of the Securities and Exchange Commission after six (6) months by holders who are not officers, directors or five percent (5%) owners of the Company's Shares. Officers, directors and 5% owners of the Company's Shares may sell Shares purchased by the exercise of the Class A or B Warrants, if any, publicly pursuant to Rule 144 after six (6) months, subject to certain volume limitations.

- 4. The Undersigned acknowledges and represents as follows:
  - (a) That he has accessed information on the Company and its products on its website, www.cardiomedics.com, and received and carefully reviewed the Offering Circular, Part II of the above mentioned Registration Statement.
  - (b) That he understands the Shares are speculative and involve a high degree of risk, he is able to bear the economic risk of the investment in the Shares, and swears that he is a bona fide resident of or domiciled in the State of \_\_\_\_\_.
  - (c) That he has, or together with his investor representative has, such knowledge and experience in financial and business matters that he is capable of evaluating the merits and risks of the prospective investment in the Shares and that he is able to bear such risks. If the undersigned has designated an "investor representative" within the meaning of Regulation D under the Securities Act of 1933, as amended, to advise him with respect to an investment in the Shares, the investor representative is:

(Telephone:	).	
/ · - · -  - · · · · · · ·		

- (d) That he understands the Shares being offered have not been registered for sale with the securities regulatory authorities of any State and may not be registered with the regulatory authorities of the State in which the Undersigned resides or is domiciled. If the Shares are not so registered, the Undersigned understands that this Subscription Agreement will not be accepted by the Company and the funds will be promptly returned to the Undersigned, without interest thereon.
- (e) That he understands an investment in the Shares is highly speculative but believes that the investment is suitable for him based upon his investment objectives and financial needs, and he has adequate means for providing for his current financial needs and personal contingencies and has no need for liquidity of the Shares.
- (f) That he has been given access to full and complete information regarding the Company (including the opportunity to meet with and ask questions of and receive

answers from Company officers and review all Company contracts and other relevant documents) and has utilized such access to his satisfaction for the purpose of obtaining information in addition to, or verifying information included in, the Offering Circular. The Undersigned understands and agrees that forward looking statements, within the meaning of Section 27A of the U.S. Securities Act of 1993 and Section 21E of the Securities and Exchange Act of 1934, in the Offering Circular cannot be assured by the Company, and the Company's actual results and future events may differ materially from those described in the Offering Circular.

		☐ natural person, ☐ sole proprietorship, ☐ partnership, on, ☐ trust or ☐
5.	The Undersigned r	represents and warrants that the answers to the following questions are check only one box and supply all requested information):
		A non-accredited person or entity.
		An accredited entity or person and the total purchase price for the Shares does not exceed 20% of the Undersigned's and his/her spouse's present worth.
		A bank as defined in section 3(a) (2) of the Act whether acting in its individual or fiduciary capacity.
		An insurance company as defined in section 2(13) of the Act.
		An investment company registered under the Investment Company Act of 1940 or a business development company as defined in section 2(a) (48) of that Act.
		A Small Business Investment Company licensed by the U.S. Small Business Administration under section 301(c) or (d) of the Small Business Investment Act of 1958.
		An employee benefit plan within the meaning of Title I of the Employee Retirement Income Security Act of 1974, if the investment decision is made by a plan fiduciary, as defined in section 3(21) of such Act, which is either a bank, insurance company, or registered investment adviser, or if the employee benefit plan has total assets in excess of \$5,000,000.
		A private business development company as defined in section 202(a)(22) of the Investment Advisers Act of 1940.
		An organization described in section 501(c)(3) of the Internal Revenue Code with total assets in excess of \$5,000,000.
		A director or executive officer of the Company.

An entity in which all of the equity owners are accredited investors under paragraph (a)(1), (2), (3), (4), (6), or (7) of Rule 501 of Regulation D promulgated under the Act. (Each equity owner must submit a signed statement verifying that he is an accredited investor.)

The Undersigned hereby represents that: (check one box)

\$50,000 \$50,000 \$50,000  \$100,000 \$100,000  \$200,000 \$200,000  (ii) He reasonably expects his yearly income (excluding his spouse's income) from all sources in 2009 to be in excess of (check highest number applicable):  \$50,000 \$100,000 \$200,000  His individual net worth, or his joint net worth with his spouse, at fair market value (including home, furnishings and personal automobiles) as of the date hereof is (check correct alternative):  Less than \$100,000 \$500,000 to \$750,000  \$100,000 to \$250,000 \$750,000 to \$1,000,000  \$250,000 to \$500,000 Over \$1,000,000  (iv) The portion of his net worth as shown above which is in liquid assets (cash, marketable securities or assets readily convertible to cash) is (check correct alternative):  Less than \$50,000 \$100,000 to \$500,000	(i)	His <u>yearly</u> income (excluding his each of 2005 and 2006 was i applicable):	spouse's income) from all sources for n excess of (check highest number
\$100,000 \$200,000    \$200,000 \$200,000    \$200,000 \$200,000    He reasonably expects his yearly income (excluding his spouse's income) from all sources in 2009 to be in excess of (check highest number applicable):    \$50,000 \$100,000 \$2200,000    His individual net worth, or his joint net worth with his spouse, at fair market value (including home, furnishings and personal automobiles) as of the date hereof is (check correct alternative):    Less than \$100,000 \$500,000 to \$750,000    \$100,000 to \$250,000 \$750,000 to \$1,000,000    \$250,000 to \$500,000 Over \$1,000,000    The portion of his net worth as shown above which is in liquid assets (cash, marketable securities or assets readily convertible to cash) is (check correct alternative):    Less than \$50,000 \$100,000 to \$200,000		<u>2007</u>	2008
\$200,000 \$200,000  (ii) He reasonably expects his yearly income (excluding his spouse's income) from all sources in 2009 to be in excess of (check highest number applicable):  \$50,000 \$100,000 \$200,000  (iii) His individual net worth, or his joint net worth with his spouse, at fair market value (including home, furnishings and personal automobiles) as of the date hereof is (check correct alternative):  Less than \$100,000 \$500,000 to \$750,000  \$100,000 to \$250,000 \$750,000 to \$1,000,000  (iv) The portion of his net worth as shown above which is in liquid assets (cash, marketable securities or assets readily convertible to cash) is (check correct alternative):  Less than \$50,000 \$100,000 to \$200,000		\$ 50,000	\$ 50,000
(iii) He reasonably expects his yearly income (excluding his spouse's income) from all sources in 2009 to be in excess of (check highest number applicable):  \$ 50,000 \$100,000 \$200,000  His individual net worth, or his joint net worth with his spouse, at fair market value (including home, furnishings and personal automobiles) as of the date hereof is (check correct alternative):  Less than \$100,000 \$500,000 \$750,000  \$100,000 to \$250,000 \$750,000 to \$1,000,000  \$250,000 to \$500,000 Over \$1,000,000  (iv) The portion of his net worth as shown above which is in liquid assets (cash, marketable securities or assets readily convertible to cash) is (check correct alternative):  Less than \$50,000 \$100,000 to \$200,000		\$100,000	\$100,000
income) from all sources in 2009 to be in excess of (check highest number applicable):  \$\[ \] \\$ 50,000 \] \\$100,000 \] \\$200,000  (iii) His individual net worth, or his joint net worth with his spouse, at fair market value (including home, furnishings and personal automobiles) as of the date hereof is (check correct alternative):  \$\[ \] Less than \\$100,000 \] \\$500,000 to \\$750,000  \$\[ \] \\$100,000 to \\$250,000 \] \\$750,000 to \\$1,000,000  (iv) The portion of his net worth as shown above which is in liquid assets (cash, marketable securities or assets readily convertible to cash) is (check correct alternative):  \$\[ \] Less than \\$50,000 \] \\$100,000 to \\$200,000		\$200,000	\$200,000
(iii) His individual net worth, or his joint net worth with his spouse, at fair market value (including home, furnishings and personal automobiles) as of the date hereof is (check correct alternative):  Less than \$100,000 \$500,000 to \$750,000  \$100,000 to \$250,000 \$750,000 to \$1,000,000  \$250,000 to \$500,000 Over \$1,000,000  (iv) The portion of his net worth as shown above which is in liquid assets (cash, marketable securities or assets readily convertible to cash) is (check correct alternative):  Less than \$50,000 \$100,000 to \$200,000	(ii)	income) from all sources in 200	
market value (including home, furnishings and personal automobiles) as of the date hereof is (check correct alternative):  Less than \$100,000 \$500,000 to \$750,000  \$100,000 to \$250,000 \$750,000 to \$1,000,000  \$250,000 to \$500,000 Over \$1,000,000  (iv) The portion of his net worth as shown above which is in liquid assets (cash, marketable securities or assets readily convertible to cash) is (check correct alternative):  Less than \$50,000 \$100,000 to \$200,000		\$ 50,000 \$100,00	\$200,000
\$100,000 to \$250,000 \$750,000 to \$1,000,000  \$250,000 to \$500,000 Over \$1,000,000  (iv) The portion of his net worth as shown above which is in liquid assets (cash, marketable securities or assets readily convertible to cash) is (check correct alternative):  Less than \$50,000 \$100,000 to \$200,000	(iii)	market value (including home, f	urnishings and personal automobiles)
\$250,000 to \$500,000 Over \$1,000,000  (iv) The portion of his net worth as shown above which is in liquid assets (cash, marketable securities or assets readily convertible to cash) is (check correct alternative):  Less than \$50,000 \$100,000 to \$200,000		Less than \$100,000	\$500,000 to \$750,000
(iv) The portion of his net worth as shown above which is in liquid assets (cash, marketable securities or assets readily convertible to cash) is (check correct alternative):  Less than \$50,000 \$100,000 to \$200,000		\$100,000 to \$250,000	\$750,000 to \$1,000,000
(cash, marketable securities or assets readily convertible to cash) is (check correct alternative):  Less than \$50,000 \$100,000 to \$200,000		\$250,000 to \$500,000	Over \$1,000,000
	(iv)	(cash, marketable securities or	
\$200,000 to \$100,000		Less than \$50,000	\$100,000 to \$200,000
\$50,000 to \$100,000		\$50,000 to \$100,000	\$200,000 to \$500,000
Greater than \$500,000			Greater than \$500,000

All of the foregoing information which the Undersigned has provided concerning the undersigned, the Undersigned's financial position and the Undersigned's knowledge of financial and business matters, or, in the case of a corporation, partnership, trust, sole proprietorship or other entity, concerning the knowledge of financial and business matters of the person making the investment decision on behalf of such entity, is correct and

complete as of the date set forth at the end hereof, and, if there should be any adverse change in such information prior to the Undersigned's Subscription Agreement being accepted, the Undersigned will immediately provide the Company with such information.

<ol> <li>The Undersigned is representations, and the</li> </ol>	aware of the sig ey are made with the	nificance to the Company of the foregoing intention that the Company will rely upon them.
7. Type of Ownership Des	ired (check one)	
Individual Ownership		Joint Tenants with Rights of Survivorship (both parties must sign)
Trust or Estate (describe and enclose evidenc of authority)	:e	Corporation (describe and enclose evidence of authority)
Partnership (dese		Other (describe below:
WITNESS the due execution h	nereof as of this	_day of, 2009.
Name Typed or Printed		Name Typed or Printed
Business or Residence Addres	SS	Business or Residence Address
City, State and Zip Code		City, State and Zip Code
Tax Identification or Social Secur	ity Number	Tax Identification or Social Security Number
Office Phone ( )		Office Phone ( )
Home Phone ( )		Home Phone ( )
Fax Number ( )		Fax Number ( )
Email		Email
Signed:		Signed:
Title, if any:		Title, if any:

6.

Date:	, 2009	Date:	, 2009
ACCEPTANCE:			
This Subscription hereby accepted	by the above named Subsas of, 2	scriber for Shares of the Co 2009 to the extent of	ompany in the above Offering is Shares.
		CARDIOMEDIC	S, INC.
		By: John McCall President	um

# CARDIOMEDICS, INC. Form 1-A Registration Statement

**EXHIBIT 11** 

**OPINION OF COUNSEL** 

#### **SMITH & ASSOCIATES**

411 SANTA MONICA BLVD. SUITE B SANTA MONICA, CALIFORNIA 90401

March 30, 2009

U.S. Securities and Exchange Commission 100 F Street Washington, D.C. 20549

Re: Offering of Cardiomedics, Inc. Pursuant to Regulation A

To Whom It May Concern:

As counsel to Cardiomedics, Inc., we have been requested to deliver to you our opinion with respect to the sale of an aggregate of up to 5,000,000 shares of common stock (the "Shares") of Cardiomedics, Inc. at a price of \$1.00 per Share. It is our opinion that these Shares are exempt from registration under the Securities Act of 1933 (the "Act") pursuant to the Section 3(b) of the Act and Regulation A promulgated thereunder. Further, it is our opinion that the Shares, when issued, delivered and sold in the manner described in the Offering Circular, will be validly issued, fully paid and non-assessable.

This opinion is being provided to you in connection with the sale of the Shares and may not be relied upon by any other person for any other purpose.

We hereby consent to the use of our name in the Registration Statement and Offering Circular, and we also consent to the filing of this opinion as an Exhibit thereto.

Very truly yours,

John Holt Smith of Smith & Associates

# CARDIOMEDICS, INC. Form 1-A Registration Statement

**EXHIBIT 15** 

**COPIES OF PUBLICATIONS** 

# External Counterpulsation Produces a Significant Reduction in Stable Angina Class, Episodes, Medication Use, and Hospitalization

The authors performed a multicenter, retrospective assessment of data from 58 patients with Canadian Cardiovascular Society (CCS) functional class II (n=27), class III (n=23), or class IV (n=8) chronic, stable angina and documented coronary artery disease who were serially treated with the CardiAssistTM External Counterpulsation System (ECP) (Cardiomedics, Inc., Irvine, CA). All of the patients received 30-35 treatments of one hour/day over a 6-7-week period. The ECP System reduced angina in CCS class II, class III, and class IV stable angina patients by an average of one CCS class, lowered the incidence of anginal episodes in 91% of the patients (53 of 58), and resulted in a 96% reduction in the number of patients requiring hospitalization for angina, from 24 in the 6 months pretreatment to one patient in the 6 months post-treatment. (CVR&R. 2001; 22:154–158) \$2001 by Cardiovascular Reviews & Reports, Inc.

Gerald Weisfogel, MD; Martin Schaffer, MD; Dietmar Gann, MD; Berge Dadourian, MD; Timothy Marshall, MD; V. Allymadian, MD† From Metuchen Heart Associates, PA, Metuchen, NJ; Nevada Cardiology Associates, Las Vegas, NE; Tucson Heart Group, Tucson, AZ; and Orange County Thoracic & Cardiovascular Surgeons, Orange, CA\*

Address for correspondence/reprint requests: Gerald Weisfogel, MD, ECP Center of New Jersey, 42 Throckmorton Avenue, Old Bridge, NJ 08857 Manuscript received June 29, 2000; accepted July 31, 2000 External counterpulsation (ECP) is a noninvasive treatment for coronary artery disease. The CardiAssist ECP System employs the sequential inflation of pneumatic cuffs about the calves, thighs, and buttocks to augment diastolic pressure and increase venous return to the heart, decreasing left ventricular afterload. Augmenting diastolic pressure increases coronary artery perfusion pressure and possibly enhances coronary collateral development, resulting in the reduction or elimination of the ischemia associated with episodes of angina.

## Historical Perspective

The concept of counterpulsation was first introduced in the U.S. in 1953, when Kantrowitz and Kantrowitz! proposed that elevation of aortic diastolic pressure could improve coronary blood flow and benefit patients with coronary insufficiency. Several early ECP devices increased coronary blood flow and demonstrated hemodynamic benefits. However, their usefulness in clinical practice has been limited because of numerous obstacles, including patient comfort, risk of electric shock, and economics. The first ECP systems consisted of a hydraulically driven device with water-filled bladders that were wrapped around the lower legs and thighs.

# ECP in Acute Myocardial Infarction

In 1972, Mueller et al.<sup>2</sup> first studied the use of ECP in the treatment of uncomplicated myocardial infarction (MI). ECP was associated with increases in diastolic pressure and in coronary blood flow. Later, Parmley et al.<sup>3</sup> demonstrated that combining the use of nitroprusside and ECP provided greater benefits than the use of either agent alone. ECP reversed the decrease in diastolic arterial pressure produced by nitroprusside-induced vasodilatation and augmented the cardiac index.

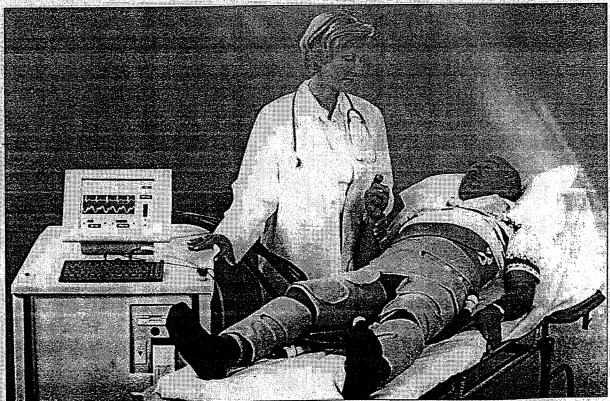
## ECP in the Treatment of Angina

Over the past two decades, a number of studies have suggested the efficacy of ECP in the treatment of patients with chronic stable angina. 4-7 The first sham-controlled study, reported by Clapp et al. 8 in 1974, using a predecessor of the current CardiAssist System, demonstrated improvement in functional classification, nitrate usage, and double product. In a subsequent study published in 1999, Arora et al. 9 concluded that enhanced ECP (EECP®, distributed by Vasomedical, Inc., Westbury, NY) reduced angina and extended time to exercise-induced ischemia in 139 patients with symptomatic coronary artery disease (CAD); exercise duration increased in both active groups, but not significantly. 9

#### Methods

Subjects. At four cardiology practices that served as study sites (see Appendix), data were collected on every patient treated with the CardiAssist™ ECP System between June, 1997 and April, 1999 who met the following criteria: age 40–90 years; angina classified as Canadian Cardiovascular Society (CCS) functional class II, III, or IV; documented evidence of CAD; and 30–35 1-hour treatments with the CardiAssist™ System. Docu-

mentation of CAD required that a patient have at least one of the following: angiographically proved stenosis of greater than 70% in at least one of the major arteries, and/or a history of MI documented by characteristic creatinine kinase elevation and development of Q waves on electrocardiography. Data were extracted from treatment forms used by each of the sites that administered the CardiAssist™ treatment regimen. When the treatment form did not provide the necessary data, they were obtained at the study site from the patient's complete medical record. The study sites routinely exclude patients from treatment if they have any of the following: CCS class I or unstable angina; MI or CABG in the preceding 3 months; cardiac catheterization in the preceding 2 weeks; overt congestive heart failure or a left venuicular ejection fraction of <30%; blood pressure of >180/100 mm Hg; a permanent pacemaker or implantable defibrillator; significant valvular heart disease; a history of varicosities, deep vein thrombosis, phlebitis, or stasis ulcer; atrial fibrillation or frequent ventricular premature beats; bleeding diathesis; or current pregnancy. CCS class III and IV patients were selected who were not surgical candidates because their conditions were inoperable or they were at high risk of operative complications or postoperative failure, had coronary anatomy that was not readily amenable to such proce-



CardiAssistM ECP offers new hope for chronic angina patients.

dures, or had comorbid conditions that created excessive risk. CCS class II patients were selected according to the same criteria or if they refused interventional procedures.

CardiAssist™ ECP System. The CardiAssist™ System is an enhanced version of the original ECP device (Cardiomedics, Inc., Irvine, CA). The system consists of a console containing air compressors, a computerized touch screen control console, valves, hoses, and three sets of cuffs. Prior to the beginning of a treatment session, the cuffs are wrapped around the patient's legs and buttocks and fastened with Velcro® (DuPont Corporation). Pressure is applied via compressed air to the cuffs in the following sequence: calves, thighs, and buttocks, in synchronization with the "r" wave of the patient's electrocardiogram. This propels arterial blood back to the coronary arteries and heart muscle. Before the end of diastole, all air is released simultaneously from all cuffs by removal of the externally applied pressure. This allows the compressed arteries and veins to reconform, reducing vascular impedance. Pressures that can be applied range from 0-310 mm Hg. Patients in this study received 250-310 mm Hg pressure. Blood pressure changes were monitored by finger plethysmography. Assessment of the hemodynamic effect of the CardiAssist" System is calculated via the device's Central Processing Unit (CPU), using the systolic and diastolic peak wave heights. A systolic to diastolic ratio equal to or greater than 1 (diastolic pressure equal to or greater than systolic pressure) is generally considered therapeutic. In this study, the average diastolic to systolic pressure ratio was 1.1 (high of 1.9, low of 0.4).

End Points. CCS functional class was determined prior to treatment and compared mathematically to the ending CCS class. Angina episodes, rehospitalization for angina, and angina medication consumption were recorded daily. During the treatment period of 6-7 weeks, events were tabulated and reported at the conclusion of treatments as "increased," 'decreased," or "no change." The average frequency of angina episodes per day was computed by dividing the total number of angina episodes over a 1week period both pre- and post-treatment. In addition, the difference in frequency of angina episodes between pretreatment and the end of treatment was calculated as percentage change and categorized as follows: 50%+, 25%-49%, and 0%-24% improvement. No patient's condition was worse after treatment; all patients treated with the CardiAssist™ System in this study displayed improvement in at least one of the parameters listed above.

Statistical Analysis. Analysis of variance, pretreatment vs. post-treatment, was performed to determine the F ratio, as well as a single variable test with a 0.05 level of significance. Changes in the incidence of angina episodes from pre- to post-treatment and thorough follow-up were analyzed by analysis of variance, and differences between groups with respect to percentage changes in the number of angina episodes were determined. Other observed factors (rehospitalization for angina, angina medication consumption, and CCS classification) were also assessed by computing percentage changes.

Number	58 10 10 10 10 10 10 10 10 10 10 10 10 10
Age in years (mean±SD) Male Female	(70±10) 42 (72%) 16 (28%)
Cardiovascular History	
CCS functional class	
<b>n</b>	27 (46%)
m M	23 (40%)
Previous CABG	8 (14%) 15 (26%)
Prévious PTCA	14 (24%)
Multiple procedures	9 (16%)
Cardiovascular Medications	
Nitrates	51 (88%)

	TABLE II. CANADIAN CARDIOLOGY SOCIETY FUNCTIONAL CLASSIFICATION	
1	NUMBER PRETREATMENT FUNCTIONAL CLASS POST-TREATMENT FUNCTIONAL CLASS F YALUE	-
ľ	58 2.67±0.71 1.71±0.65 7.32 x 10-12	

TABLE III. PERCENT IMPROVEMENT IN ANGINA SYMPTOMS	
Number 50+% 25%-49% 0%-24%	
58 42	

TABLE IV. AVERAGE NUMBER OF ANGINA EPISODES OVER 24 HOURS	
NUMBER PRETREATMENT ANGINA P. VALUE	
58 1.59±2.86 0.31±0.57 0.001	

TABLE V. HOSPITALIZATIONS PER PATIENT OVER 6 MONTHS OF FOLLOW-UP
TABLE V. HOSPITALIZATIONS PER PATIENT OVER 0 MONTHS OF TOLEGONS
NUMBER PRETREATMENT POST-TREATMENT P VALUE
24 - 1.17±038 0.04±0.20 1.02 x 10-16

#### Results

Patient Characteristics. Of the 58 patients, 54 received 35 1-hour treatments over a 7-week period. Four patients received <35 treatments (30, 31, 33, and 34). The average age was 70 (oldest, 90; youngest, 47). Forty-two patients were male (72%) and 16 female (28%). Twentyseven patients were CCS class II (46%), 23 were CCS class III (40%), and eight were class IV (14%). Twentynine of the 58 patients (50%) had undergone prior invasive procedures, such as coronary artery bypass grafting (CABG) or angioplasty. Nine patients (16%) had previously undergone multiple CABG, percutaneous transluminal coronary angioplasty (PTCA), and/or stenting. These data are shown in Table I.

CCS Functional Class. Changes in functional class are shown in Table II. The eight class IV patients improved by an average of 1.7 CCS classes (4.0 to 2.3). There was a 44% average improvement in the class IV patients (50% improvement in six and 25% improvement in the remaining two patients). The 23 class III patients improved by an average of 0.9 class (3.0 to 2.1), the average improvement being 29% (four showed no improvement, 18 showed 33% improvement, and one showed an improvement of 67%). The 27 class II patients improved by an average of 0.8 class (2.0 to 1.2). There was 41% improvement on average among the 27 class 11 patients (22 showed an improvement of 50%, while five patients showed no improvement). All of the eight CCS class IV patients, 83% of class III patients (19 of 23), and 81% of class

II patients (22 of 27) improved in terms of CCS functional classification. For the entire group of 58 patients, the CCS class was reduced from 2.67 to 1.71. Overall, 84% of the patients (49 of 58) experienced a reduction in their CCS classifications, while 16% (nine of 58) showed no improvement.

Angina Incidence. Fifty-three of the 58 patients (91%) experienced a reduction in their angina episodes posttreatment, from an average of 1.59±2.86 episodes per 24-hour period to 0.31±0.57 episodes per 24-hour period. Forty-two of the 58 patients (72%) had a significant decrease in the number of angina episodes and were calculated to have achieved 50%+ improvement. Eleven patients (19%) showed a 25%-49% reduction in angina episodes, while five patients (9%) fell into the 0%-24% category. No patient had an increase in the frequency of angina episodes. These results are given in Tables III and IV.

Hospitalization Incidence. Twenty-three of the 24 patients (96%) who had been hospitalized in the 6-month period before treatment reduced their hospitalization rate for angina to zero in the 6 months following treatment (Table V).

Nitroglycerin Usage. As detailed in Table VI, consumption of angina medication (expressed as the number of times taken per 24 hours) decreased by 77.4%, from an average of 0.62 ± 0.71 pretreatment to an average of 0.14±0.33 post-treatment.

	TABLE VI. SUB	LINGUAL NI	TROCLYCE	RIN CONSUMPT	ION PER DAY		
1	NUMBER	PRET	REATMENT	P	OST-TREATMENT	( )	ALUE
	58	.0.6	52±0.71		0.14±0.33	7.94	x 10-6

2	
CLASS	Description
Class 1	Ordinary physical activity does not cause angina. Angina with strenuous, rapid, or prolonged exertion at work or recreation.
Class II	Slight limitation of ordinary activity.  Angina with walking or climbing stairs rapidly. Walking uphill, walking or stair climbing after meals.  Walking in cold or wind, or under emotional stress. During the few hours after awakening. Walking more than two blocks on level ground and climbing more than one flight of ordinary stairs at a normal pace and under normal conditions.
Class III	Marked limitation of ordinary physical activity.  Angina with walking 1-2 blocks on level ground and climbing one flight of stairs under normal conditions and at a normal pace.
Class IV	Inability to carry on any minimal physical activity without discomfort. Anginal syndrome may be present at res

#### Discussion

Study Limitations. The sample size was relatively small and this study was not randomized or blinded. The long-term effects of ECP on symptoms and clinical events are unknown, although it is encouraging that 14–24 months post-treatment most patients continue to have relief. Despite the lack of controls, the results actually reflect a lack of bias, as the studied cohort was a population treated consecutively based on accepted inclusion/exclusion criteria for patients at very high risk for additional operative procedures or whose anatomy was not amenable to invasive procedures. All patients who met the inclusion criteria were treated. The findings of this study mirror many of the recently reported results of the MUlticenter STudy of Enhanced ECP (the MUST-EECP trial), 9 a prospective, randomized, blinded study.

Possible Clinical Implications. CAD is chronic in nature. Normally, long-term survival can be extended if some type of secondary intervention/prevention can be applied. The practitioners in these study centers routinely see patients with recurrent stable angina despite current or previous therapy with anti-ischemic agents and various revascularization attempts. The patients in this study fall into this category and thus it would seem that ECP may offer an additional treatment option.

#### Conclusion

One of the authors' motivations was to determine if daily application of ECP therapy in a normal clinical setting would produce results similar to those obtained in a controlled, scientific study setting. Despite the shortcomings mentioned above, it is comforting to have found that an ECP system applied in a real-world treatment setting provided excellent results for a large angina patient population. A body of data, including this study, demonstrates that ECP, delivered pneumatically in a sequential manner via cuffs encircling the lower extremities (calves, thighs, and buttock area), is an effective therapy for patients with chronic stable angina.

Appendix: ECP Center of New Jersey, 42 Throckmonton Avenue, Old Bridge, NJ 08857, 732-679-7972—Nevada Cardiology Associates, 3150 N. Tenya Way, Ste. 460, Las Vegas, NV 89128, 702-233-1000—Tucson Heart Group, 4892 North Stone, Tucson, AZ 85704, 520-696-4780—Orange County Thoracic and Cardiovascular Surgeons, 1310 West Stewart Drive, Ste. 502, Orange, CA 92868, 714-997-2224.

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#### ORIGINAL PAPER

## New Graduated Pressure Regimen for External Counterpulsation Reduces Mortality and Improves Outcomes in Congestive Heart Failure: A Report From the Cardiomedics External Counterpulsation Patient Registry

External counterpulsation (ECP) has been shown to increase exercise tolerance and reduce angina episodes, Canadian Cardiovascular Society Functional (CCSF) class, anginal medication usage, and hospitalizations in refractive CCSF class III and IV stable angina. However, the high pressures and resulting 1.5:1-2:1 peak diastolic to peak systolic pressure (D/S) ratios shown to be optimal in the treatment of angina can cause excessive preload and adverse effects in congestive heart failure (CHF) patients, particularly those with left ventricular ejection fractions <40%. Data were retrospectively analyzed from the Cardiomedics ECP Registry on 127 New York Heart Association (NYHA) class II-IV CHF patients (79.6% men; average age ± SD, 68.2±15.6 years), with a comorbidity of CCSF class III-IV refractive angina, who were serially treated with 35 hours of ECP (1 h/d, 5 d/wk for 7 weeks) at unconventionally low pressures and D/S ratios under a new graduated pressure regimen. The pressures and D/S ratios were gradually increased in stages over the 7-week ECP regimen. The patients were divided into three groups based on the pressures applied and the resulting average D/S ratios (Low, Mid, and High). In the Low D/S ratio group (average D/S ratio 0.7:1), all-cause mortality in the year following ECP treatment was only 1.85% (one of 54 patients), whereas over the same time period in the Mid D/S ratio group (average D/S ratio 1.08:1), all-cause mortality was 7.69% (three of 39 patients) and in the High D/S ratio group (average D/S ratio 1.32:1), all-cause mortality was 8.82% (three of 34 patients). For the Low, Mid, and High D/S ratio groups, respectively: 1) average left ventricular ejection fractions increased 23.0%, 20.1%, and 17.5%; 2) NYHA class declined 36.6%, 29.6%, and 29.6%; and 3) all-cause hospitalizations, including terminal admissions, were reduced 85.7%, 82.6%, and 57.1% in the year following ECP therapy from the prior year. There were no adverse effects or withdrawals from the ECP therapy and no significant difference in sex-based outcomes. Consequently, ECP applied at low pressures and average D/S ratios of 0.7:1 under the new graduated pressure regimen is safe and effective in the treatment of CHF and produces a significant reduction in mortality, compared with the 8.5% annualized mortality of the Multicenter Automatic Defibrillator Implantation Trial II (MADIT II) (N=1232) of NYHA class II-III CHF and the 12.2% annual mortality of the Comparison of Medical Therapy, Pacing, and Defibrillation in Heart Failure [COMPANION] study [N=595] of NYHA class III-IV CHF. Lower pressures improve patient comfort and may encourage more CHF patients to seek treatment. The reduction in hospitalizations should significantly reduce the cost of treating CHF. (CHF. 2005;11:147-152) \$2005 CHF, Inc.

a noninvasive version of the intraaortic balloon pump. However, the ECP device used in this study moves a significantly larger volume of blood than an intra-aortic balloon pump. ECP decreases cardiac workload while increasing myocardial perfusion pressure and cardiac output. The use of ECP for the outpatient treatment of angina pectoris has been shown to reduce the frequency of chest pain episodes, increase exercise tolerance, reduce the incidence of hospitalization, and reduce Canadian Cardiovascular Society Functional (CCSF) class in intractable angina.<sup>1</sup>

Cardiovascular hemodynamics would ordinarily indicate that congestive heart failure (CHF) patients with a left ventricular ejection fraction

Krishnaswami Vijayaraghavan, MD; Lawrence Santora, MD; Joel Kahn, MD; Norman Abbott, MD; Julius Torelli, MD; Gil Vardi, MD6 From the Scottsdale Cardiovascular Center, Scottsdale, AZ; Orange County Heart Institute, Orange, CA; Michigan Heart Group, Troy, MI; Palms Heart Center, Tarpon Springs, FL; Integrative Cardiology Center, High Point, NC; and St. Louis Heart and Vascular, St. Louis, MO6

Address for correspondence: Krishnaswami Vijayaraghavan, MD, Scottsdale Cardiovascular Center, 3099 Civic Center Plaza, Scottsdale, AZ 85251.

E-mail: kvijay@scresearch.org

Manuscript received December 23, 2004; accepted January 24, 2005.

may - June 2005

147

(LVEF) <40% would be less likely to benefit from ECP and, if treated with ECP, might be expected to experience an exacerbation of heart failure symptoms, as ECP compresses the venous beds in the lower extremities, increasing venous return (preload). Increased preload, particularly in CHF patients with an LVEF <40%, could potentially cause adverse events, including worsening of pulmonary heart failure,2 increased morbidity and mortality,34 and premature withdrawal from ECP therapy.5 However, little data are available on the long-term effects of ECPapplied at unconventionally low peak diastolic to peak systolic pressure (D/S) ratios which are gradually increasedin the treatment of CHF.

#### Objective

This study seeks to analyze the effects of 35 1-hour ECP treatments applied at lower than customary D/S ratio levels in graduated stages over a period of 7 weeks, compared with conventional ECP D/S ratio levels, on mortality, LVEF, New York Heart Association (NYHA) CHF class and the incidence of all-cause hospitalization over a period of 1 year, compared with baseline and prior year data.

#### Methods

Study Population. The Cardiomedics ECP Patient Registry is a compendium of data on all patients undergoing ECP at the reporting sites. Data from this registry on a series of 127 NYHA class II-IV CHF patients with a comorbidity of CCSF class III-IV angina, consecutively treated with ECP at six clinical sites in the United States, were retrospectively analyzed. Patients were enrolled in the registry if they met the inclusion criteria: 1) between 20 and 80 years of age; 2) documented evidence of coronary artery disease; 3) coronary arteries not amenable to further percutaneous or surgical revascularization; 4) symptoms of intractable angina with inadequate response to medical therapy; and 5) symptoms and signs of CHF with shortness of breath, leg edema, or significant fatigue.

All patients received medical therapy consistent with conventional clinical practice, and 35 1-hour ECP treatments with the CardiAssist ECP System (Cardiomedics, Inc., Irvine, CA) for 1 h/d, 5 d/wk over a period of 7 weeks. One-year follow-up data were collected on all patients.

The 127 CHF patients were divided into three groups based upon the pressures applied in stages during the 35 1-hour ECP treatments and their resulting average D/S ratios. Pressures and D/S ratios were applied at uncommonly low levels (starting as low as 0.1:1), based on the patient's LVEF and response to ECP, and gradually increased in small increments in stages over the 35-hour, 7-week ECP regimen, under a new "Graduated Pressure Regimen" (patent pending) developed by the manufacturer of the ECP System used in this study.

The 54 CHF patients in the Low D/S ratio group were treated at an average D/S ratio of 0.7:1 (range 0.40:1–0.99:1) over the 7-week ECP regimen. The 39 CHF patients in the Mid D/S ratio group were treated at an average D/S ratio of 1.08:1 (range 1.00:1–1.29:1) over the same period. The 34 CHF patients in the High D/S ratio group were treated at an average D/S ratio of 1.32:1 (range 1.30:1–1.60:1) over this period, which is comparable to the D/S ratios commonly used in the treatment of angina.

Study End Points. The study end points were comparative changes in mortality, LVEF, NYHA CHF class, and incidence of all-cause hospitalizations (including terminal hospitalizations) of the three groups during a period of 1 year following ECP therapy, compared with baseline and the 1-year period preceding ECP therapy.

Statistical Analysis. Data on enrolled patients were collected at six clinical sites and entered into a standardized Excel database (Microsoft Corporation, Redmore, WA). The final dataset was merged and transferred to an SPSS 12.0 statistical package (SPSS Inc., Chicago,

IL). Data were analyzed on each group of CHF patients and comparisons made pretreatment and 1-year post-treatment. Measurements were expressed as mean  $\pm$  SD. Individual variable differences were determined using the Student t test for numerical variables and the chi-square test for categorical variables, with significance at p < 0.05.

Baseline Data. Baseline characteristics of the three groups are shown in Table I. Of the 54 CHF patients in the Low D/S ratio group, 79.6% were men, and the mean age was 68.2±15.6 years. Six (11.1%) had class II CHF, 42 (77.8%) had class III CHF, and six (11.1%) had class IV CHF. CCSF class III angina was present in 76.8%, and 24.3% also had CCSF class IV angina. Mean LVEF before ECP therapy was 32.6%±7%. History of coronary artery bypass graft surgery was present in 75.9% and history of percutaneous transluminal coronary angioplasty was present in 90.7%.

Of the 39 CHF patients in the Mid D/S ratio group, 79.5% were men, and the mean age was 69.7±18.6 years. Nine (22.5%) had class II CHF, 24 (60.0%) had class IV CHF. CCSF class III angina was present in 79.8%, and 14.3% also had CCSF class IV angina. Mean LVEF before ECP therapy was 31.3%±11%. History of coronary artery bypass graft surgery was present in 69.6% and history of percutaneous transluminal coronary angioplasty was present in 83.4%.

Of the 34 CHF patients in the High D/S ratio group, 82.4% were men, and the mean age was 69.7±22.4 years. Thirteen (36.1%) had class II CHF, 15 (41.6%) had class III CHF, and six (16.6%) had class IV CHF. CCSF class III angina was present in 74.5%, and 19.3% also had CCSF class IV angina. Mean LVEF before ECP therapy was 32.6%±20%. History of coronary artery bypass graft surgery was present in 78.9% and history of percutaneous transluminal coronary angioplasty was present in 80.9%.

The patients in all three groups received medical therapy in accordance with accepted medical practice.

Table 1. Baseline Patient Characteristics by Study Groups

		STUDY GROUP	
CHARACTERISTIC	LOW D/S RATIO (N=54)	MID D/S RATIO (N=39)	High D/S RATIO (N=34)
Average age (yr ± SD)	68.2±15.6	69.7±18.6	69.7±22.4
Men (n [%])	43 (79.6)	31 (79.5)	28 (82.4)
Women (n [%])	11 (20.3)	8 (20.0)	6 (17.6)
History of CABG (%)	75.9	69.6	78.9
History of PTCA (%)	90.7	83.4	80.9
Ejection fraction (% ± SD)	33±7	31±11	33±20
NYHA CHF class II (n [%])	6 (11.1)	9 (22.5)	13 (36.1)
NYHA CHF class III (n [%])	42 (77.87)	24 (60.0)	15 (41.6)
NYHA CHF class IV (n [%])	6 (11.1)	6 (15.0)	6 (16.6)
Angiolensin-converting enzyme inhibitors (%)	81.5	55.0	74.4
Beta blockers (%)	31.4	30.3	23.3
Diuretics (%)	68.5	55.0	<i>7</i> 5.0
Calcium channel blockers (%)	11.1	15.2	9.3
Nitroglycerin (%)	66.3	62.4	61.2

D/S=peak diastolic to peak systolic pressure; CABG=coronary artery bypass graft surgery; PTCA=percutaneous transluminal coronary angioplasty; NYHA=New York Heart Association; CHF=congestive heart failure

STUDY GROUP (NYHA CLASS)	MORTAUTY (%)	COMPARISON GROUP (NYHA CLASS)	Mortality (%)	P VALUE
Low D/S ratio (II-III)	0.00	MADIT II (II-III)	8.50	<0.0001
Low D/S ratio (III-IV)	2.10	COMPANION (III-IV)	12.20	<0.0001
Low D/S ratio (II-IV)	1.85	Mid D/S (II-IV)	7.69	<0.0001
Low D/S ratio (II-IV)	1.85	High D/S (II-IV)	8.82	< 0.0001
Mid D/S ratio (II-IV)	<i>7.5</i> 0	High D/S (II-IV)	8.33	NS

NYHA=New York Heart Association; D/S=peak diastolic to peak systolic pressure; MADIT II=Multicenter Automatic Defibrillator Implantation Trial II study; COMPANION=Comparison of Medical Therapy, Pacing, and Defibrillation in Heart Failure study; NS=not significant

None of the 127 patients had an LVEF >40% or <20% (Table I).

#### Outcomes

Mortality. In the year following completion of ECP therapy, of the 54 CHF patients in the Low D/S ratio group (average D/S ratio 0.70:1), one class IV patient (1.85%) died at age 67 of CHF. Of the 39 CHF patients in the Mid D/S ratio group (average D/S ratio 1.08:1), three patients (7.69%) died (one class III and two class IV) at ages 62, 66, and 75 of CHF, cardiogenic shock, and sepsis, respectively. Of the 34 CHF patients in the High D/S ratio group (average D/S ratio 1.32:1), three class IV patients (8.82%) died at ages 49, 66, and 76 of cardiogenic shock, cardiogenic shock, and sepsis, respectively.

Of the 48 NYHA class II-III CHF patients in the Low D/S ratio group,

none (0%) died in the year following ECP therapy, compared with the 8.5% mortality (adjusted to a 1-year period) reported in the Multicenter Automatic Defibrillator Implantation Trial II (MADIT II)6 of an implantable defibrillator in the treatment of 1232 NYHA class II and III CHF patients (p<0.0001). Of the 48 NYHA class III-IV CHF patients in the Low D/S ratio group, one (2.1%) died in the year following ECP therapy, an 82.8% reduction (p<0.0001) from the 12.2% 1-year, all-cause mortality reported in the Comparison of Medical Therapy, Pacing, and Defibrillation in Heart Failure (COMPANION) study<sup>2</sup> of 595 NYHA class III-IV CHF patients treated with a dual chamber pacemaker with or without an implantable defibrillator.

The 1.85% annual mortality in the 54 patients in the Low D/S ratio group

was a 75.3% reduction from the one year mortality of 7.69% in the Mid D/S ratio group (p<0.001) and a 77.8% reduction from the 8.82% 1-year mortality in the High D/S ratio group (p<0.0001).

There was no statistical difference in annual mortality between the Mid and High D/S ratio groups (Table II).

Ejection Fraction. LVEF was assessed by echocardiography before and 1 year after ECP treatment. Of the 53, 36, and 31 surviving patients in the Low, Mid, and High D/S ratio groups and the 123 surviving patients of the group as a whole, LVEFs improved by 23.0%, 20.1%, 17.5%, and 20.4%, respectively, one year after ECP therapy, from a mean of 32.6% to 40.1%, 31.3% to 37.5%, 32.6% to 38.3%, and 32.3% to 38.9%, respectively (Table III).

GROUP	BEFORE ECP (%)	YEAR AFTER ECP (%)	CHANGE (%)	P VALUE
Low D/S ratio (n=53)	32.6±7.2	40.1±26.9	+23.0	<0.05
Mid D/S ratio (n=36)	31.3±11.6	37.5±27.5	+20.1	NS
High D/S ratio (n=31)	32.6±20.4	38.3±14.7	+17.5	NS

GROUP	BEFORE ECP	YEAR AFTER ECP	CHANGE (%)	P VALUE
Low D/S ratio (n=53)	3.0±1.0	1.9±0.5	-36.6	<0.0001
Mid D/S ratio (n=36)	2.7±1.3	1.9±0.5	-29.6	<0.005
High D/S ratio (n=31)	2.7±1.3	1.9±0.5	-29.6	<0.01

GROUP	YEAR BEFORE ECP	YEAR AFTER ECP	CHANGE (%)	P VALUE
Low D/S ratio (n=54)	2.8±1.6	0.35±0.5	-87.5	<0.0001
Mid D/S ratio (n=39)	2.5±1.4	0.42±0.5	-83.2	<0.0001
High D/S ratio (n=34)	1.3±1.7	0.70±0.5	-46.2	<0.01

NYHA CHF Class. Of the 53 surviving patients in the Low D/S ratio group, NYHA class improved by an average of 36.6% from a mean class of  $3.0\pm1.0$ pretreatment to a mean class of  $1.9\pm0.5$ 1 year after ECP treatment (p<0.0001). Of the 36 surviving patients in the Mid D/S ratio group, NYHA class improved by an average of 29.6% from a mean class of 2.7±1.3 pretreatment to a mean class of 1.9 ± 0.5 I year after ECP treatment (b<0.005). Of the 31 surviving patients in the High D/S ratio group, NYHA class improved by an average of 29.6% from a mean class of 2.7±1.3 pretreatment to a mean class of 1.9±0.5 1 year after ECP treatment (p<0.01) (Table IV).

Hospitalizations. Of the 54 Low D/S ratio group patients, the average incidence of all-cause hospitalization, including terminal hospitalizations, was reduced by 87.5% from a mean admission rate of 2.8 per patient in the year before ECP treatment to 0.35 per patient in the following year (p<0.0001). Of the 39 Mid D/S ratio group patients, the average incidence of all-cause hospitalization, including terminal hospitalizations, was reduced by 83.2% from a

mean admission rate of 2.5 per patient in the year before ECP treatment to 0.42 per patient in the following year (p<0.0001). Of the 34 High D/S ratio group patients, the average incidence of all-cause hospitalization, including terminal hospitalizations, was reduced by 46.2% from a mean admission rate of 1.3 per patient in the year before ECP treatment to 0.7 per patient in the following year (p<0.01) (Table V).

As seen in Table IV, the incidence of hospitalization was significantly reduced in all NYHA CHF classes in both the Low D/S ratio and Mid D/S ratio groups in the year following ECP therapy, compared to baseline (p<0.0001). However, in the High D/S ratio group, the change in NYHA CHF class was not significant in CHF Class II and was less significantly improved in the Class III and IV CHF patients (p<0.0001).

Sex-Based Differences. While mortality in the year following ECP therapy in women was 7.7% (1 of 13) and 14.3% (1 of 7) in the Low D/S ratio and Mid D/S ratio groups, respectively, compared to mortality in men of 0.0% (0 of 41) and 6.3% (2 of 32), in the High

D/S ratio group, mortality in men was 6.9% (2 of 29) vs. mortality in women of 0.0% (0 of 5) in the year following ECP therapy. No assessment of statistical significance was performed due to the small samples and disparity in population sizes. There were no significant sex-based differences in LVEFs, NYHA CHF class, or incidence of hospital admissions (Table VII).

#### Discussion

ECP is a noninvasive, nonpharmacologic therapy that has been shown to be of benefit in reducing the number of anginal episodes, exercise-induced myocardial ischemia, CCSF class, and incidence of hospitalization in patients with chronic stable angina. However, due to concern over the increased preload resulting from ECP and its potential to worsen heart failure symptoms in patients with CHF, 2-5 particularly those with LVEFs < 40%, data on the use of ECP in the treatment of patients with left ventricular dysfunction is sparse.

In previous studies, 2-5 CHF patients treated with an ECP device (EECP, Vasomedical, Inc., Westbury, NY) were shown to be more likely to experience an adverse cardiac event, less

may - June 2005

Table VI. Average Number of All-Cause Hospitalizations by New York Heart Association (NYHA) Class HOSPITALIZATIONS P VALUE NYHA CLASS YEAR BEFORE ECP YEAR AFTER ECP CHANGE (%) GROUP < 0.0154 1.33 0.17 -88.5 6 Low D/S ratio 11 < 0.0001 0.38 -87.8 Ħ 42 3.08 < 0.0154 0.38 -84.0 IV 6 2.38 NS -94.4 1.78 0.11 Mid D/S ratio 1 Ó <0.0001 -81.4 111 24 2.46 0.46 < 0.005 -78.6 IV 9 2.33 0.50 -15.0NS 1.0 0.85 11 13 High D/S ratio 0.79 0.36 -54.5 < 0.01 m 14 0.9 --68.9 NS IV 2.9 ECP=external counterpulsation; D/S=peak diastolic to peak systolic pressure; NS=not significant

Group	AVERAGE AGE (YR)	MORTALITY (% [N])	LVEF CHANGE (%)	NYHA CHANGE (%)	HOSPITALIZATION CHANGE (%
Low D/S ratio					
Men (n=41)	68.5	0.0 (0)	+24.1	-26.6	<b>-85.5</b>
Women (n=13)	65.2	7.7 (1)	+20.8	-25.8	<b>-87.3</b>
Mid D/S ratio					
Men (n=32)	68.9	6.3 (2)	+16.8	-24.1	-80.8
Women (n=7)	74.9	14.3 (1)	+22.2	-34.5	-94.2
High D/S ratio					
Men (n=29)	70.7	6.9 (2)	+20.2	-32.1	<b>50.0</b>
Women (n=5)	66.4	0.0 (0)	+15.4	-33.3	-55.6

likely to benefit from ECP, have a higher likelihood of morbidity and mortality, and were more likely to prematurely withdraw from the 35-hour 7-week ECP treatment regimen. Exacerbation of CHF symptoms was the most frequent reason for non-completion of the ECP regimen.

The present study is the first to report a significant reduction in allcause mortality in NYHA class II-IV CHF patients in the year following 35 1-hour ECP treatments over a period of 7 weeks, under a new, graduated pressure regimen, starting at D/S ratios as low as 0.1:1. Incremental increases in pressures and D/S ratios were made in stages during the 35-hour course of therapy. The average D/S ratios over the 35-hour course of ECP therapy under the new regimen in the Low and Mid D/S ratio groups were substantially lower than D/S ratios commonly used in the treatment of angina.

One-year all-cause mortality in the 48 NYHA class II-III CHF patients

in the Low D/S group was zero, compared with the adjusted annual mortality of 8.5% in the 1232 NYHA class II–III CHF patients of the MADIT II study<sup>6</sup> of an implantable defibrillator. One-year all-cause mortality in the 48 NYHA class III–IV CHF patients in the Low D/S ratio group was 2.1%, an 82.8% reduction from the 12.2% annual all-cause mortality in the 595 NYHA class III–IV CHF patients in the COMPANION study<sup>7</sup> of a dual chamber pacemaker with or without an implantable defibrillator.

One-year all-cause mortality of 1.85% in the Low D/S ratio group (average D/S ratio 0.7:1) was 75.33% lower than the 1-year all-cause mortality of 7.50% in the Mid D/S ratio group (average D/S ratio 1.08:1) and 77.8% less than the 1-year, all-cause mortality of 8.33% in the High D/S ratio group (average D/S ratio 1.32:1).

While the present study is small compared with the very large population of NYHA class II-IV CHF patients addressed in the American Heart Association's Heart Failure and Stroke 2002 Statistical Update,<sup>6</sup> the 1.85% 1-year mortality in the Low D/S ratio group was 90% lower than the historical 18.8% annual mortality from CHF reported in the 2002 Statistical Update, which included NYHA class I patients, who typically experience little or no mortality.

In addition, at I year, there was a significant increase from baseline in mean LVEFs and a significant reduction from baseline in mean NYHA CHF class, as well as a significant reduction in the average incidence of hospital admissions in the year following ECP treatment, compared with the year before ECP. The Low D/S ratio group had the greatest increase in LVEFs, reduction in CHF class, and decline in hospitalizations.

Mortality in women in this study (8.0%) was higher than in men (4.9%). However, the population sizes were small and of disparate sizes

(25 vs. 102). If these mortality rates are confirmed by a larger study, it may indicate the need for earlier and more appressive ECP and medical therapy in women with CHF.

The safery of the ECP device used in this study is demonstrated by there having been no adverse events and no patient withdrawals during or following ECP therapy. The lower pressures employed to produce the Low D/S ratios increased patient comfort and made ECP more tolerable.

The benefits of ECP in the treatment of CHF noted in this study may be due to a variety of factors. In addition to the new graduated ECP regimen's theoretical potential to train the heart to accept and eject increasing volumes of blood and, perhaps, training the ventricles to beat more synchronously, improvement in endothelial function is believed to result from increased shear forces.9 The release of endogenous growth factors10 is thought to cause angiogenesis and increased vascularity of the myocardium. An increase in NO production<sup>11</sup> may potentially be another therapeutic effect. Other hypotheses for the efficacy of ECP include enhancement of vascular reactivity, neurohormonal alteration, stimulation of protein kinases, and alteration of myocyte metabolism at the cellular level.

The present study is limited in that it is a retrospective analysis with no control group, and the population is small. No efforts were made to maximize the use of neurohormonal blocking agents before enrollment. In spite of this, the average utilization of angiotensin-converting enzyme (ACE) inhibitors at baseline was 63.8% and β blockers 30.7% in this study population. It is possible that some of the NYHA class IV patients could not tolerate either of these agents, thus creating an opportunity to use ECP therapy as a bridge to initiate and/or up-titrate the administration of B blockers and ACE inhibitors, resulting in a reduction in mortality.

Other caveats to this study include the variability of subjective assessment of NYHA class, the variability of thresholds for hospitalization for CHF in different parts of the country, and interobserver variability of echocardiographic interpretations of LVEFs (±5%).

In spite of these limitations, the present study clearly demonstrates the significant benefits, efficacy, and safety of ECP administered at average D/S ratios

of 0.7:1 in the treatment of CHF under the new graduated pressure regimen. While additional data from prospective, controlled clinical studies would be desirable, ethics may preclude randomization of CHF patients to a control group, in light of the reduction in mortality demonstrated in this study.

#### Conclusion

ECP, rendered under the new graduated pressure regimen utilized in this study at unconventionally low pressures and average D/S ratios of 0.7:1, is safe and efficacious in the treatment of CHF and significantly reduces mortality, increases LVEFs, improves CHF functional status, and reduces hospital admissions over a period of 1 year following completion of ECP therapy. The use of lower pressure under the new regimen increases the patient's ability to tolerate ECP therapy and could encourage more heart failure patients to be treated, and the reduction in hospital admittances could significantly lower the cost of treating CHF.

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# Heart Failure 1

(ICD/9 428) (ICD/10 I50)

#### Prevalence

• Overall estimated 2004 prevalence of heart failure (HF) in adults age 20 and older: 5,200,000 (2,600,000 males, 2,600,000 females).

#### Incidence

- Based on the 44-year follow-up of the NHLBI's FHS (Hurst W. The Heart, Arteries and Veins. 10th ed. New York, NY: McGraw-Hill; 2001)...
  - HF incidence approaches 10 per 1,000 population after age 65.
  - Seventy-five percent of HF cases have antecedent hypertension.
- Based on 1971–96 data from the NHLBI's FHS (Circulation. 2002;106:3068-3072)...
  - At age 40, the lifetime risk of developing congestive heart failure (CHF) for both men and women is one in five.
  - At age 40, the lifetime risk of CHF occurring without antecedent MI is one in nine for men and one in six for women.
  - The lifetime risk doubles for people with blood pressure greater than 160/90 mm Hg versus those with blood pressure less than 140/90 mm Hg.
- A community-based cohort study conducted in Olmsted County, Minnesota, showed that the incidence of HF (ICD9/428) has not declined during two decades, but survival after onset has increased overall, with less improvement among women and elderly persons. (JAMA. 2004;292:344-350.)

#### **Risk Factors**

- Data from the FHS indicate that hypertension is a very common risk factor for HF and it contributes to a large proportion of HF cases. (JAMA. 1996;275:1557-1562.)
- A study of the predictors of HF among women with coronary heart disease found that diabetes was the strongest risk factor. (Circulation. 2004;110:1424-1430.)
- The prevalence of diabetes is increasing among older persons with HF, and diabetes is a significant independent risk factor for death in these individuals. Mayo Clinic researchers found that the odds of having diabetes for those first diagnosed with HF in 1999 was nearly four times higher than those diagnosed 20 years earlier. (N Engl J Med. 2006;355:251-259.)

#### Mortality

- Heart failure, estimated 2004 mortality 57,700.
- Based on the 44-year follow-up of the NHLBI's FHS...
  - Eighty percent of men and 70 percent of women under age 65 who have HF will die within eight years.
  - After HF is diagnosed, survival is poorer in men than in women, but fewer than 15 percent of women survive more than eight to 12 years. The one-year mortality rate is high, with one in five dying.
  - In people diagnosed with HF, sudden cardiac death occurs at six to nine times the rate of the general population.
- From 1994–2004, deaths from HF increased 28 percent. In the same time period, the death rate declined 2.0 percent. (NCHS and NHLBI)
- The 2004 overall death rate for HF was 19.1.

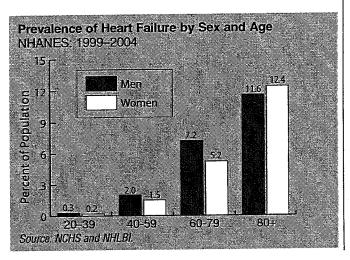
  Death rates were 20.3 for white males, 22.9 for black males, 18.3 for white females and 19.0 for black females. (NCHS and NHLBI)

#### **Hospital Discharges**

• Hospital discharges for HF rose from 399,000 in 1979 to 1,099,000 in 2004, an increase of 175 percent. (NHDS, NCHS and NHLBI)

#### Cost

• The estimated direct and indirect cost of HF in the United States for 2007 is \$33.2 billion.



# Clinical Assessment of External Pressure Circulatory Assistance in Acute Myocardial Infarction

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EZRA A. AMSTERDAM, MD, FACC\*
JOHN BANAS, MD, FACC†
J. MICHAEL CRILEY, MD, FACC‡
HENRY S. LOEB, MD, FACC\$
HILTRUD MUELLER, MD, FACC\$
JAMES T. WILLERSON, MD, FACC\$
DFAN T. MASON, MD, FACC\*

From the Departments of Medicine and Physiology, University of California School of Medicine, Davis, California and Medical Center, Sacramento, California\*; Tufts-New England Medical Center Boston, Massachusetts†; Harbor General Hospital, Torrance, California‡; U.S. Veterans Administration Hospital, Hines, Illinois; Loyola University Stritch School of Medicine, Chicago, Illinois§; St. Louis University School of Medicine, St. Louis, Missouri and Southwestern Medical School-Parkland Memorial Hospital, Dallas, Texas¶. Manuscript received August 6, 1979; revised manuscript received September 25, 1979, accepted September 26. 1979.

Other participating investigators in the cooperative study: H. Beanlands, MD, Toronto Western Hospital, Toronto, Ontario, Canada; M. Broder, MD, . Cleveland Metropolitan Hospital, Cleveland; M. H. Ellestad, MD, Memorial Hospital Medical Center, Long Beach, California; M. Ende, MD, Petersburg General Hospital, Petersburg, Virginia; S. A. Forwand, MD, Mount Auburn Hospital, Cambridge. Massachusetts; A. D. Hagan, MD, Naval Regional Medical Center, San Diego, California; P. Lavine, MD, Hahnemann Medical College and Hospital, Philadelphia, Pennsylvania, J. V. Messer, MD, Rush-Presbyterian-St. Luke's Medical Center, Chicago, Illinois; J. Morch, MD, Toronto General Hospital, Toronto, Ontario, Canada; T. Nivatpumin, MD, Montefiore Hospital, New York, New York; A. Obeid, MD, Veterans Administration Hospital, Syracuse, New York; E. Perlstein, MD, Rancocas Valley Hospital, Willingboro, New Jersey; S. H. Rahimtoola, MD, University Hospital, Portland, Oregon; E. Rapaport, MD, San Francisco General Hospital, San Francisco, California; I. Schatz, MD, University Hospital, Ann Arbor, Michigan; J. Schroeder, MD, Stanford University Medical Center, Stanford, California; S. Smith, MD, University of Colorado Medical Center, Boulder, Colorado; W. Towne, MD, Cook County Hospital, Chicago, Illinois; W. Tuttle, MD, Shadyside Hospital, Pittsburgh, Pennsylvania.

Address for reprints: Ezra A. Amsterdam, MD, Departments of Medicine and Physiology, University of California School of Medicine, Davis, California 95616.

The clinical effects of early application of external pressure circulatory assistance (EPCA) in acute myocardial infarction were evaluated in a prospective, randomized trial involving 258 patients in 25 institutions. All patients had mild left ventricular failure and received circulatory assistance within the first 24 hours after the onset of symptoms. There were no significant differences between the treatment and control groups, consisting of 142 patients and 116 patients, respectively, with regard to age, sex, race, previous cardiac history, electrocardiographic location of myocardial infarction, Norris prognostic index, admission heart rate, blood pressure and chest roentgenogram, and time from onset of symptoms to hospital admission. There were also no differences between the treatment and control groups with regard to antiarrhythmic, positive inotropic, diuretic and vasodilator therapy. Hospital mortality was significantly decreased, compared with that of control patients, in the group receiving 4 or more hours of external pressure circulatory assistance within the first 24 hours after admission (mortality rate 6.5 percent [7 of 108] in treatment group versus 14.7 percent [17 of 116] in control group, p < 0.05). Circulatory assistance for 3 or more hours was also associated with a lower mortality rate in the subgroup (patients 46 or more years old) to which mortality in this study was confined (mortality rate 8.3 percent [9 of 109] in the treatment group versus 17.5 percent [17 of 97] in the control group, p < 0.05). For the combined group of patients with 3 or more and 4 or more hours of treatment, circulatory assistance was associated with significant lessening (p <0.05 to <0.01) of morbidity as manifested by recurrent chest pain, progression of cardiac failure, occurrence of ventricular fibrillation, change in heart size and clinical cardiac functional status at discharge. These data support further application and investigation of external pressure circulatory assistance in myocardial infarction.

As a result of advances in the management of cardiac arrhythmias in coronary care units, the major cause of mortality in patients hospitalized with acute myocardial infarction is cardiac pump dysfunction, manifested by severe left ventricular failure or cardiogenic shock.<sup>1</sup> This complication is directly related to loss of a critical mass of myocardium that is usually extensive, commonly involving 40 percent or more of the left ventricle.<sup>2–4</sup> Recent experimental and clinical studies<sup>5,6</sup> of myocardial infarction have demonstrated that therapeutic interventions that favorably alter the balance between myocardial oxygen supply and demand can reduce ischemic cardiac injury and limit infarct size. This approach thus has the potential of improving prognosis in acute myocardial infarction by preserving cardiac tissue and averting complications, such as pump failure, that are related to extent of myocardial damage.

Improvement in the relation between myocardial oxygen supply and demand can be achieved by increasing availability of oxygen or reducing

its requirement. Mechanical circulatory assistance elevates myocardial oxygen delivery by augmentation of arterial diastolic pressure, a major determinant of coronary blood flow, which assumes special importance in the maintenance of myocardial perfusion in the presence of obstructive narrowing of the coronary arteries. 7 Diastolic pressure augmentation can be effected by invasive techniques such as intraaortic balloon counterpulsation<sup>8-14</sup> or noninvasive external counterpulsation.8,9,15,16 The latter approach has the advantages of wide applicability, ease of implementation and lack of associated trauma. Early intervention with mechanical circulatory assistance prior to the onset of severe cardiac dysfunction has been suggested 10-12 and recently applied<sup>14</sup> as a potential means of preserving myocardium, averting pump failure and reducing mortality in acute myocardial infarction. This report presents the results of a multicenter trial to evaluate the clinical effects of external pressure circulatory assist by a mechanical device (Cardiassist® External Counterpulsation System, Cardiassist Corporation, Hoffman Estates, Illinois) in patients with acute myocardial infarction complicated by mild left ventricular failure (Killip class II).<sup>17</sup>

#### Methods

Patients: Twenty-five cooperating institutions participated in the study, which was carried out over a 15 month period. The population evaluated consisted of 258 patients with acute myocardial infarction. The mean number of patients per institution was 9, and the range was one (two institutions) to 26 (one institution) patients per institution.

Diagnosis of myocardial infarction was by two of the three following criteria: classic history, characteristic electrocardiographic evolutionary changes and typical serum enzyme alterations. All patients fulfilled the following criteria, in addition to acute myocardial infarction, for admission to the

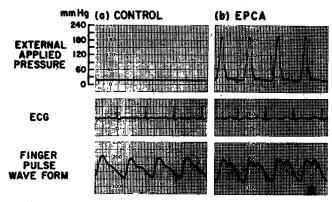


FIGURE 1. Top panel, actual external pressure applied during counterpulsation. Middle panel, electrocardiogram (ECG). Bottom panel, finger pulse waveform recorded from finger plethysmography depicting relative changes (uncalibrated). Data are recorded with patient in the external pressure circulatory assistance (EPCA) device before (a) and during (b) augmentation of diastolic pressure. The delays in transmission of central arterial pressure to the limbs and in transmission of peripheral externally applied pressure centrally account for the temporal relations between applied pressure and the finger pulse waveform. The water required to fill the leg unit accounts for the external pressure before activation of external pressure (a) and during the inactive phase of counterpulsation (b).

study: mild left ventricular failure (Killip class II),<sup>17</sup> manifested by pulmonary rales over less than 50 percent of the lung fields; entrance into the study within 19 hours of onset of symptoms (with the goal of completion of at least 4 hours of circulatory assistance within the first 24 hours of myocardial infarction); absence of history of previously treated cardiac failure; and absence of clinical evidence of peripheral vascular disease and aortic valve insufficiency. All patients gave informed consent for entrance into the study. Allocation of patients to treatment and control groups was by random assignment as described in the Appendix.

Evaluation of left ventricular function: Left ventricular functional status on admission and during the subsequent hospital course was classified by clinical and roentgenographic criteria. Clinical classification was made according to the following criteria<sup>17</sup>: class I, absence of clinical complications, clear lung fields; class II, rales over less than 50 percent of the lung fields; class III, pulmonary edema with rales over 50 percent or more of the lung fields; and class IV, shock manifested by criteria for class III plus a systolic blood pressure of less than 90 mm Hg with signs of inadequate peripheral organ perfusion (diaphoresis, cyanosis, oliguria, altered mental status). Chest roentgenograms were interpreted and classified by a radiologist without knowledge of clinical classification: class I, normal lung fields; class II, redistribution of pulmonary blood flow to the upper lung fields and mild hilar congestion; class III, criteria for class II plus marked increase in prominence of pulmonary vessels of the outer lung fields; and class IV, criteria for class III plus presence of pleural effusion, and hilar congestion or cardiomegaly, or both.

Roentgenographic determination of heart size was performed on admission and on the day of, or 1 day before discharge. This evaluation 18 was based on the extent to which the transverse cardiac diameter exceeded that resulting in a cardiothoracic ratio of 0.5: normal, transverse cardiac diameter of up to 1.0 cm in excess of the latter criterion; questionable cardiac enlargement, increase in transverse cardiac diameter of more than 1.0 to 1.5 cm in excess of this criterion; definite cardiac enlargement, increase in transverse cardiac diameter of more than 1.5 cm in excess of this criterion. This analysis was included in the evaluation midway through the study and was therefore available in some patients.

External pressure circulatory assistance: Circulatory assistance was administered to the treatment group only. Each hour of treatment consisted of 50 minutes of circulatory assistance and 10 minutes of rest. There were no restrictions on any other available forms of therapy for patients in either the treatment or the control group.

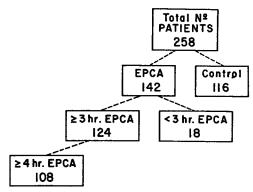


FIGURE 2. Number of patients in the control group and the groups with external pressure circulatory assistance. The number of hours indicates the total time of circulatory assistance in the first 24 hours after the onset of symptoms of myocardial infarction.

External pressure circulatory assistance was administered by a device that encloses the lower limbs from thigh to ankle in a hydraulically activated leg unit. External counterpulsation was delivered through the controlled application of positive external pressure by the leg unit. The device did not include a negative pressure phase. The timing, magnitude and duration of external pressure were each regulated to produce the desired diastolic augmentation. Diastolic augmentation was assessed by indirect recording of finger pulse waveform by a volume-sensing finger plethysmograph, with which each device is equipped (Fig. 1). Counterpulsation was effected by synchronization of mechanical activation with the electrocardiogram to produce positive pressure during diastole. The technique was applied to achieve maximal diastolic augmentation, which resulted in elevation of peak pressure during diastole to levels approximating systolic pressure (Fig. 1). External pressures ranged up to 250 mm Hg for a duration of up to 250 ms to produce satisfactory diastolic augmentation. The maximal duration of 250 ms was selected because prior experience indicated it to be the maximum necessary to produce the desired effect over a wide range of heart rates.

Evaluation of data: All data were recorded and maintained in individual patient books at each institution. A copy of the completed data record was forwarded to a central office where it was reviewed and evaluated by the project steering committee, consisting of the authors. All data were evaluated without knowledge of whether the patients were in the treatment or the control group.

Statistical analysis was performed by application of the chi square test to categorized variables and Student's two-tailed t test to continuous variables.

#### Results

Duration of treatment: Two hundred fifty-eight patients fulfilled the study criteria; 116 of the patients

TABLE I
Mortality Rate in Control Group and Patients Treated With
External Pressure Circulatory Assistance (EPCA)

	Total	Control Group	Treat- ment Group	р
All treated patients* vs.				
control group	258	116	142	
Patients (n) Deaths (n)	29	17	12	
Mortality rate (%)	20	14.7	8.4	NS
Patients with ≥3 h EPCA in first 24 h vs. control group				
Patients (n)	240	116	124	
Deaths (n)	26	17	9	
Mortality rate (%)		14.7	7.3	NS
Patients ≥ 46 yr with ≥3 h EPCA in first 24 h vs. control group				
Patients (n)	206	97	109	
Deaths (n)	26	17	9	
Mortality (%)		17.5	8.3	<0.05
Patients with ≥4 h EPCA in first 24 h vs. control group				
Patients (n)	224	116	108	
Deaths (n)	24	17	7	
Mortality (%)		14.7	6.5	<0.05

<sup>\*</sup> Includes 18 patients who received less than 3 hours of external pressure circulatory assistance within the first 24 hours after onset of myocardial infarction. NS = not significant; p = probability.

constituted the control group and 142 the treatment group. Of the latter patients, 108 received 4 or more hours of external pressure circulatory assistance (mean 5.0 hours, maximum 8.1 hours) completed within the first 24 hours after the onset of symptoms of myocardial infarction and 124 received the assistance for 3 or more hours (mean 4.7 hours, maximum 8.1 hours) within the first 24 hours (Fig. 2). Eighteen patients in the treatment group received less than 3 hours of treatment in the first 24 hours.

Time from onset of symptoms to completion of treatment: This interval was determined for the group receiving 4 or more hours of treatment. Completion of 4 or more hours of external pressure circulatory assistance was achieved within 12 hours of onset of symptoms in 31 patients (29 percent), within 18 hours in 45 patients (42 percent) and within 24 hours in 32 patients (29 percent). Therefore, treatment was completed within 18 hours of onset of symptoms in 71 percent of patients.

Hospital mortality: Mortality did not differ significantly (p > 0.05) from that of the control group for the total group of 142 patients who received external pressure circulatory assistance and for the group that received 3 or more hours of assistance in the first 24 hours (Table I). However, mortality was significantly less than that of the control group for those patients aged 46 or more years (the population in this study in which mortality occurred) who received 3 or more hours of circulatory assistance in the first 24 hours (8.3 versus 17.5 percent, p < 0.05) and for the entire group that received 4 or more hours of assistance in the first 24 hours (6.5 versus 14.7 percent, p <0.05) (Table I). In addition, mortality from cardiac pump failure alone was significantly less than in the control patients for both the entire group that received 3 or more hours of circulatory assistance (5.7 versus 13.8 percent, p < 0.04) and the group that received 4 or more hours of treatment (4.6 versus 13.8 percent, p <0.02) (Table II). There were no significant differences in proportion of deaths due to primary cardiac arrhythmias in the treated and control

Specific subgroups of patients considered to be at increased risk were analyzed in regard to the effects of external pressure circulatory assistance on mortality. These subgroups consisted of patients with transmural myocardial infarction, anterior infarction, and a Norris index<sup>19</sup> greater than 6. (The Norris index is described in the Appendix.) For these analyses, the treatment

TABLE II

Mortality Rate in Control and Patient Groups

Cause of Death	Control Group	Patients With ≥3 h EPCA	p	Patients With ≥4 h EPCA	p
Pump failure		5.7%	<0.04*	4.6%	<0.02*
Arrhythmia	(16/116) 0.9% (1/116)	(7/124) 1.6% (2/124)	NS*	(5/108) 1.9 % (2/108)	NS

<sup>\*</sup> Compared with control group. Abbreviations as in Table I.

TABLE III

Comparison of Clinical Data on Admission of Control Group and Patients Aged 46 or More Years Treated With 3 or More Hours of External Pressure Circulatory Assistance

		Age (yr)					Sex Race			Ca	rdiac H	istory			ECG Location of MI			
Group	<b>₹</b> 50			60–69	≥70	M	F	W	NonW	AP	N	Al E	30th	Neithe	er A	nt	Inf	Nontrans
Control n %	9 (9.3)	41 (42		35 (36.1)	12 (12.4)	78 (80.4)	19 (19.6)	82 (85.4)	14 (14.6	25 ) (25.	10 8) (10		2 22.7)	40 (41.2	56 ) (5		35 36.1)	6 (6.2)
Treatment n %	13 (11.9	50 9) (45		32 (29.4) 2	14 (12.8)	94 (86.2) >0.			11 (10.3) 0.3	26 (23.	8) (7.5		0  8.4) 	55 (50.5	54 ) (49		45 41.3) >0.2	10 (9.2)
<u> </u>		HR (be	ate/m	in)		Svs	tolic BP	(mm H	a)			Radiogr	aphic	Class			orris Inc	
Group	<60	60-79	80-9	9 ≥10	0 <100	100-109			0–129	≥130	ı	11	III	IV	V	4-<6	6-<8	3 ≥8
Control n %	7 (7.4)	32 (34.0)	33 (35.1	22 ) (23.4	6 I) (6.2)	8 (8.2)	14 (14.4			56 (57.7)	17 (19.1)	67 (75.3)	2 (2.2)	3 (3.4)	4 (4.1)	26 (26.8)	36 (37.1	31 ) (32.0)
Treatment n %	6 (5.7)	30 (28.3)	41 (38.	29 7) (27.	6 I) (5.5)	8 (7.3)	12 (11.0 >0	)) (		67 (61.5)	23 (22.1)		9 (8.6) >0.1	1 (1.0)	5 (4.6)	33 (30.3)	46 ) (42.2 )>0.5	

Ant = anterior; AP = angina pectoris; BP = blood pressure; ECG = electrocardiographic; HR = heart rate; Inf = inferior; MI = myocardial infarction; NonW = nonwhite; Nontrans = nontransmural; p = probability; W = white.

group consisted of patients receiving 3 or more hours of circulatory assistance. Mortality in treated patients with transmural myocardial infarction was 7.1 percent (8 of 113) compared with 15.4 percent (17 of 110) in the control group (p <0.05). Although mortality tended to be lower in the treatment group with anterior infarction (8.5 percent, 5 of 59) than in the control group (16.4 percent, 11 of 67), this difference was not significant (p >0.05). In patients with a Norris index greater than 6, the treated group had a significantly lower mortality rate, 9.6 percent (7 of 73) versus 22.7 percent (17 of 75), (p <0.04).

Clinical characteristics and time from onset of symptoms to admission (Tables III, IV and V): There were no significant differences on admission with re-

spect to the broad set of clinical characteristics assessed between the control group and the subgroup of patients aged 46 or more years with 3 or more hours of treatment, the entire group with 3 or more hours of treatment, or the entire group with 4 or more hours of treatment. In addition, the mean time from onset of symptoms to admission to the coronary care unit was similar in the treatment and control groups: 6.9 versus 7.2 hours (p >0.05).

Cardiac complications: Morbidity, as defined by several cardiac complications, was significantly less in each of the total treatment groups completing 3 or 4 or more hours of external pressure circulatory assistance, respectively, within the first 24 hours after onset of symptoms of myocardial infarction than in the control

TABLE IV

Comparison of Clinical Data on Admission of Control Group and All Patients Treated With 3 or More Hours of External Pressure Circulatory Assistance

	Ans	(vr)			Sex Race (			Cardia	c Histo	ry	ECG Location of MI				
<50			≥70	M	F	W	NonW	ĀΡ	Mi	Both	Neither	Ant	Inf	Nontr	ans
							40	00	44	0.4	50	67	12	6	
28 (24.1)	41 (35.3)					99 (86.1)	16 (13.9)	(25.0)	(9.5)	(20,7)	(44.8)				
28 (22.6)			14 (11.3)			106 (86.9)	16 (13.1) 0.8	29 (23.4)			63 (50.8)	59 (47.6)			
			<u>:</u>			olic BP (m	m Ha)		Ra	diogra	ohic Class		Norris	Index 19	)
<60				<100				≥130	1	II	III IV	<4			
7 (6.2)	40 (35.4)	41 (36.3)	25 (22.1)	6 (5.2)	9 (7.8)	19 (16.4)	17 (14.7)	65 (56.0)	21 (19.6	78 ) (72.9)	5 3 ) (4.7) (2.8)	7 (6.0)	34 (29.3)		32 (27.6)
8 (6.6)	36 (29.8)	43 (25.5)	34 (28.1)	6 (4.8)	10 (8.1)	13 (10.5) >0.7	18 (14.5)	77 (62.1)	28 (23.5			8 (6.4)		(37.9)	26 (21.0
	28 (24.1) 28 (22.6) <60	28 41 (24.1) (35.3) 28 50 (22.6) (40.3)  HR (bea <60 60-79  7 40 (6.2) (35.4) 8 36	28 41 35 (24.1) (35.3) (30.2) 28 50 32 (22.6) (40.3) (25.8) >0.3  HR (beats/min) <60 60-79 80-99  7 40 41 (6.2) (35.4) (36.3) 8 36 43	$\begin{array}{c ccccccccccccccccccccccccccccccccccc$		28 41 35 12 94 22 (24.1) (35.3) (30.2) (10.3) (81.0) (19.0) 28 50 32 14 107 17 (22.6) (40.3) (25.8) (11.3) >0.3	$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$			Age (yr) Sex NonW AP Mi Both Neither Ant Sex NonW AP Mi Both Neither Ant Sex NonW AP Mi Both Neither Ant Neither Ant Neither Ant Sex NonW AP Mi Both Neither Ant	$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$

Abbreviations as in Table III.

TABLE V

Comparison of Clinical Data on Admission of Control Group and Patients Treated With 4 or More Hours of External Pressure Circulatory Assistance

				Age (y	r)		Se	x	B	ace		Card	iac Histo	ory	EC	G Loca	ation	Of MI
Group	~	50 5		9 60-		70	М	F	W	NonV	V AP	MI	Both	Neither	An	t I	nf l	Vontrans
Control																		•
n ·	28		11	35	12		94	22	99	16	29		24	52	67	43		6
%	(24	4.1) (	35.3	(30.	2) (10	0.3)	(81.0)	(19.0)	(86.1)	(13.9	) (25.0	) (9.5)	(20.7)	(44.8)	(57.	8) (3/	7.1)	(5.2)
Treatment												_	4-	ra	40	-		40
n	22		14	31			94	14	92	14	27		17	57	48	50		10
%	(20	0.4) (	40.7	(28.		0.2)	(87.0)	(13.0)	(86.8)	(13.2	2) (25.0	(6.5)	(15.7)	(52.8)	(44.		3.3)	(9.3)
р				>0.2			>0.	.8		0.8			>0.5				0.1	
			HR (	beats	/min)		S	Systolic I	3P (mm h	lg)	Ra	diograp	hic Cla	ss		Norris I	ndex	19
							100-	110-	120-						·			
Group	<60	60-7	79 80	0-99	≥100	<100	109	119	129	≥130	ı	11	III	IV ·	<4.	4-<6	6-<	38 ≥8
Control																		
n	7	40	4	1	25	6	9	19	17	65	21	78	5	3	7	34	43	32
%	(6.2)	(35.	4) (3	36.3)	(22.1)	(5.2)	(7.8)	(16.4)	(14.7)	(56.0)	(19.6)	(72.9)	(4.7)	(2.8)	(6.0)	(29.3)	(37.	0) (27.6)
Treatment	• •	•		•														
n	6	34	3	9	26	4	8	13	16	67	22	71	9	1	5	38	43	22
%	(5.7)	(32.	4) (3	37.1)	(24.8)	(3.7)	(7.4)	(12.0)	(14.8)	(62.0)	(21.4)	(68.9)		(1.0)	(4.6)			8) (20.4)
D	• •	-		>0.9					0.8			>(	0.4			>0	),5	

Abbreviations as in Table III.

group (Table VI). Data regarding change in roentgenographically determined heart size were available for 57 percent (138 patients) of the study group because of inclusion of this factor after initiation of the study.

Other medical treatment: Analysis of pharmacologic therapy during the first 5 days of hospitalization demonstrated no significant differences (p >0.05) between the groups receiving treatment (3 or more hours of treatment, age 46 or more years; total group with 3 or more hours of treatment and total group with 4 or more hours of treatment) and the control group with respect to proportion of patients receiving antiarrhythmic drugs, diuretic agents, digitalis, vasodilator drugs and propranolol and no differences with regard to analgesic or sedative therapy during the interval from 12 hours after admission through day 5. There was no relation between vasodilator therapy and the clinical outcome in either group. Data were not available for comparative analysis of therapy after day 5.

Complications of external pressure circulatory assistance: There were no complications directly attributable to this procedure. Discomfort of the lower limbs was a common complaint and some patients

complained of a distressing feeling of confinement when in the device, but there was no injury or evidence of trauma from the procedure. Pulmonary embolism, which proved fatal, occurred in one patient in the treatment group, and in none of the control group.

#### Discussion

Validity of study: This trial of application of external pressure circulatory assistance during the first 24 hours after the onset of symptoms of myocardial infarction was associated with a reduction in hospital mortality and morbidity in certain large groups of patients with acute myocardial infarction complicated by mild cardiac failure. Several aspects of this study support a relation between this treatment and the favorable clinical outcome in the treated patients. The trial was controlled by application of randomization in the selection of the study groups. This method provides several important advantages in the design of a clinical trial and contributes considerably to the significance of the results.<sup>20</sup> Randomization affords an unbiased means of selecting the treatment and control groups and is the most practical approach to eliminating or reducing

TABLE VI

Morbidity in Control Group and Groups Treated With External Pressure Circulatory Assistance (EPCA)

	≥3 h EPCA		Control			≥4 h EPCA		Control		
•	n	%	n	%	p	n	%	n	%	р
Recurrent chest pain (12 h to 5 days)	49/124	39.5	68/116	58.6	<0.01	44/108	40.7	68/116	58.6	<0.01
Progression of CHF (to class III or IV)	8/122	6.6	17/115	14/8	< 0.04	6/106	5.7	17/115	14.8	<0.03
Ventricular fibrillation	1/115	0.9	7/99	7.1	<0.02	1/101	1.0	7/99	7.1	0.04
Change in heart size					< 0.05					,
Increase	3/74	4.0	6/63	9.5		2/64	3.1	6/63	9.5	
Decrease	32/74	43.2	15/63	23.8		29/64	45.3	15/63	23.8	
No change	39/74	52.7	42/63	66.7		33/64	51.6	42/63	66.7	
Discharged class I	106/120	88.3	88/115	76.5	<0.02	92/104	88.5	88/115	76.5	< 0.03

CHF = cardiac heart failure; p = probability.

systematic differences in their characteristics. Further, this method is the most reliable means of limiting not only apparent bias in selection of study populations, but also those inapparent factors that could affect the outcome of an investigation of a therapeutic intervention. Adequacy of randomization of our patients was assessed by comparative statistical analysis of multiple risk factors related to prognosis in acute myocardial infarction. The results of the analyses are consistent with appropriate randomization, as reflected by comparable prevalence of these risk factors in the treatment and control groups on entry (Tables III to V).

With respect to the unequal number of patients per institution, we considered it mandatory to include all patients in this prospective trial in the analysis of data. Interestingly, the results of external pressure circulatory assistance were more favorable in institutions that contributed a higher number of patients than in those with fewer patients entered in the study. These differences were not significant however.

The validity of this study was supported by rigorous implementation of the protocol, randomization procedure, data acquisition and analytic methods. All patients included and excluded were reviewed and categorized at several levels of the investigation, as indicated in the Appendix, and all exclusions are accounted for. Of further importance is the representative nature of the control group in this study, in terms of hospital mortality among patients with Killip class II infarction<sup>17</sup>, indicating that the observed differences in outcome between the treatment and control patients cannot be attributed to an atypically high mortality rate in the latter.

Role of duration of therapy in reducing mortality: The beneficial clinical effects of external pressure circulatory assistance were closely related to the duration of this therapy administered in the 24 hours after the clinical onset of acute myocardial infarction. Thus, whereas evidence of benefit in patients receiving less than 3 hours of treatment was lacking, morbidity related to infarction was reduced in the groups receiving 3 or more or 4 or more hours of treatment (Table VI). Moreover, mortality in relation to that of the control patients was reduced in only a specific subgroup of the patients treated for 3 or more hours, those aged 46 or more years, whereas it was decreased in the entire group treated for 4 or more hours (Table I). These findings demonstrate enhanced clinical benefit with greater duration of external pressure circulatory assistance, suggesting a direct relation of this therapeutic intervention to the differences in outcome in the treated and control patients. Although mortality in the treated and control patients differed significantly only in the two aforementioned groups, outcome was consistently favorable in all treated groups (Table I). Mortality related to cardiac pump failure alone was significantly less in the patients treated for 3 or more hours and those treated for 4 or more hours than in the control group (Table II). In this regard, it is reasonable that a beneficial effect on survival obtained from therapy with the potential to limit infarct size might be more directly

reflected by a decrease in mortality due to pump failure than by a reduction in overall mortality.

Role of infarct size and pump failure: The most critical factor determining the clinical course of patients hospitalized with acute myocardial infarction is infarct size, because cardiac pump failure, the major cause of mortality in this setting, is the result of extensive cardiac damage.<sup>2-4</sup> The potential for limitation of infarct size has been demonstrated by interventions that improve the balance between myocardial oxygen supply and demand by decreasing oxygen consumption or increasing supply.<sup>5,6</sup> Mechanical augmentation of diastolic pressure has been utilized to achieve the latter effect. In this regard, it has been suggested that mechanical circulatory assistance may have an important role in early application to control myocardial damage before hypotension and severe cardiac pump failure develop. 10-12 This concept has recently been applied with resultant evidence of limitation of myocardial injury in the subgroup of patients with anterior myocardial infarction and residual patency of the left anterior descending coronary artery.<sup>14</sup> External pressure circulatory assistance may provide a noninvasive means to achieve this effect.

Experimental data have demonstrated that therapy to limit ischemic myocardial injury is significantly influenced by the timing of the intervention after the onset of infarction. Thus, hyaluronidase has been associated with evidence of limitation of myocardial damage after experimental canine infarction when the agent was administered within 6 hours after coronary occlusion, whereas it had no demonstrable effect when given at 9 hours.<sup>21</sup> The beneficial clinical effects of external pressure counterpulsation in our patients were associated with application of treatment at a later time than that suggested as necessary by the aforementioned study. This discrepancy can be related at least in part to factors such as the inconsistency between the experimental model of myocardial infarction and the clinical entity and the multiplicity of factors that determine infarct size in man, such as the specific coronary artery involved and the site of obstruction, the presence or absence of collateral vessels and the state of myocardial oxygen demand. Nevertheless, the importance of early intervention in myocardial infarction to impede progressive ischemic damage is clear and it is noted that more than two thirds of our patients did complete treatment within 18 hours of the onset of symptoms.

Enhancement of myocardial perfusion: role of augmentation of diastolic blood pressure: Previous studies have suggested that external pressure counterpulsation may be beneficial in ischemic heart disease by improving myocardial perfusion. This improvement could involve an increase in total coronary blood flow or a favorable redistribution of myocardial blood flow. As indicated indirectly in this study and by previous direct measurements of intraarterial pressure, 15,16 external pressure counterpulsation produces considerable augmentation of diastolic blood pressure, a critical determinant of coronary blood flow, of particular importance in the presence of obstructive coronary artery

disease. Diastolic pressure augmentation possesses the major advantage of increasing arterial pressure during the period of minimal left ventricular intramural pressure, thereby producing a maximum gradient for coronary perfusion. Enhancement of myocardial perfusion by this procedure has been suggested by studies of the technique in experimental and clinical infarction demonstrating improvement in cardiac metabolism and efficiency, <sup>22–25</sup> a reduction in S-T segment injury pattern<sup>26</sup> and augmentation of regional contractile function. <sup>27</sup> The effect on total coronary blood flow has been inconsistent <sup>16,21,22</sup> although experimental studies suggest that external pressure counterpulsation may increase coronary collateral flow to ischemic myocardium. <sup>28,29</sup>

Complications of external pressure counterpulsation: Complications were limited to discomfort of the legs, which in a few patients may preclude this therapy. However, no local trauma or lesions were evident. One patient in the treatment group had a fatal pulmonary embolism. Although dislodging of thrombi in leg veins is a theoretic hazard with this procedure, we did not find an increased incidence of this complication with this approach.

Implications: The early results of external pressure counterpulsation in this multicenter trial of patients with acute myocardial infarction and mild (class II) cardiac failure are encouraging and support further application and evaluation of this approach in other subgroups of patients with acute myocardial infarction and other forms of ischemic heart disease. Further objective assessment of the effects of this treatment on myocardial ischemia and infarct size with current methods is also warranted.

#### **Acknowledgment**

We express our appreciation to Joseph V. Messer, MD, for his efforts during the conduct of this trial and gratefully acknowledge the encouragement and suggestions of Eugene Braunwald, MD, Leon Resnekov, MD and H.J.C. Swan, MD, during the design and performance of the study. We also thank Nubar Hagopian, BSEE, MBA, for technical assistance and Leslie Silvernail and Karen Gilmore for secretarial assistance.

#### APPENDIX

Randomization procedure: All patients were assigned to the treatment or control groups by random allocation made at a central, independent coordinating center. To promote representative distribution of patients in the treatment and control groups at all institutions, a separate set of random tables was prepared for each institution and was utilized exclusively for its patients throughout the study. On presentation of a patient, assignment to either the control or treatment group was obtained by direct telephone call to the coordinating center, which was available on a 24-hour basis.

Exclusion of ineligible patients: The 258 patients who met the study criteria were obtained from a total group of 326 patients on whom randomization and admission to the protocol were requested. Of this initial total, 68 patients (39 of 181 [21.5 percent] from the treatment group and 29 of 145 [20.0 percent] from the control group) were ineligible on the basis of study criteria and were therefore excluded. The ineligible group included 39 patients who did not fulfill the criteria for acute myocardial infarction, 10 patients who did not fulfill criteria for clinical class II status, 13 patients who were not admitted within the prescribed time limit, 3 patients with insufficient data and 3 patients who were excluded because of a noncardiac death. Exclusion of 40 of these patients was made by the principal investigator at each institution. The remaining 28 patients were excluded by decision of the steering committee because of absence of criteria for diagnosis of myocardial infarction (10 patients), nonfulfillment of the time requirements for admission (13 patients) and noncardiac death (3 patients [2 in the treatment and 1 in the control group]). In addition to the evaluation of all patients excluded from the study by the institutional principal investigator and the steering committee, a review and confirmation of the validity of exclusion was made by a physician unassociated with the study.

Mortality in the ineligible patients: Analysis of mortality in the 68 patients ineligible for inclusion in the study revealed eight deaths in the 39 patients who had been allocated to the treatment group and three deaths in the 29 patients assigned to the control group. Four of the eight deaths in the treatment group were in patients who, although randomized to this group, did not receive external pressure circulatory assistance because of their early exclusion by the respective institutional investigators on the basis of failure to meet inclusion criteria. The specific reasons for exclusion of the nonsurvivors were: absence of myocardial infarction (treatment group, two patients), failure to fulfill clinical class II criteria (treatment group, three; control group, one); failure to meet time requirements for entry (treatment group, one; control group, one) and noncardiac death (treatment group, two; control group, one). Exclusion of five of the nonsurvivors, three from the treatment group and two from the control group, was made by the steering committee on the basis of failure to meet the time requirements for entry (treatment group, one patient; control group, one patient) and noncardiac death (treatment group, two; control group, one). The remaining six nonsurvivors were excluded by the respective institutional investigators because of absence of myocardial infarction (treatment group, two) and failure to fulfill class II criteria (treatment group, three; control group, one).

Norris index: The Norris index<sup>19</sup> is a prognostic index that provides a probability level for hospital mortality in patients with acute myocardial infarction on the basis of six readily measurable clinical factors on admission: (1) age, (2) electrocardiographic location of infarction, (3) systolic blood pressure, (4) heart size, (5) lung fields on roentgenography, and (6) history of myocardial ischemia. Each factor is assigned a relative weight according to the specific data, the sum of the weights equaling the index score. Mortality associated with a score of 6 to 7 is 22 percent.

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## **External Counterpulsation**

## Management of Cardiogenic Shock After Myocardial Infarction

Harry S. Soroff, MD; Charles T. Cloutier, MD; William C. Birtwell; Linda A. Begley, RN; Joseph V. Messer, MD

• Twenty patients in cardiogenic shock following myocardial infarction were treated with external counterpulsation. Eleven patients died during or soon after treatment. One patient survived for three days and another for three weeks; both died in the hospital of complications apparently unrelated to counterpulsation. Seven patients were discharged from the hospital and remained well. The patients who responded to external counterpulsation did so within the first few hours. There seemed to be no benefit in applying counterpulsation for more than six hours. Sequential analysis of mortality statistics indicated that the 45% survival rate (which included the two short-term survivors) was a significant improvement (P<.01) over the usual 15% survival rate in cases of cardiogenic shock.

(JAMA 229:1441-1450, 1974)

EXTERNAL counterpulsation (ECP)—a method of assisting the circulation without invading the vascular system—was conceived by our group, and, at the same time, by Dennis et al<sup>2</sup> and Osborn et al.<sup>3</sup> We have published many reports of results in both experimental animals and normal volunteers during the last ten years. Our studies have shown that application

of a positive pressure pulse to the lower extremities during cardiac diastole can raise the diastolic pressure by 40% to 50%, while release of pressure or application of negative pressure during cardiac systole can lower the systolic pressure by about 30%. Studies in normal volunteers and in animals have indicated that ECP increases the venous return to the heart because of the unidirectional valves in the peripheral venous bed. In cardiogenic shock accompanied by myocardial ischemia, the increased coronary flow that ECP provides may improve cardiac function and thus indirectly affect the hemodynamic response to ECP.

This report describes a cooperative study-conducted over a year's time-in which 20 patients suffering from cardiogenic shock following myocardial infarction were treated with ECP.

#### Methods

Selection of Patients.—Four women and 16 men, ages 47 to 78 years (an average of 63), were referred by physicians from nine different hospitals. Each patient's condition prior to ECP is summarized in Tables 1 and 2.

The diagnosis of cardiogenic shock. made initially by the referring physician, was based solely on conventional clinical criteria: recent myocardial infarction, low systolic blood pressure (80 mm Hg or less), oliguria (urine output of 30 ml/hr or less), cold and clammy skin, and mental lethargy or confusion. (Measurements of variables such as cardiac index, although very useful, were not available to us.) If, despite fluid-loading, a patient required drugs for more than four hours to maintain a systolic pressure of 80 to 100 mm Hg, the patient was considered a candidate for assisted circulation. Similarly, if diuretics increased the urine output but the arterial pressure remained low, the patient was treated with ECP. We did not exclude any patient whose physician thought that a trial of ECP was warranted and whose condition fulfilled our criteria.

Treatment Protocol.—Our ECP team was generally able to assemble at a patient's bedside with the ECP equipment in less than an hour, although in some cases we took as long as two hours. Meanwhile, the medical personnel in immediate charge of the pa-

Reprint requests to Department of Surgery, School of Medicine, Health Sciences Center, State University of New York at Stony Brook, Stony Brook, NY 11790 (Dr. Soroff).

From the departments of surgery (Drs. Sorott and Cloutler and Mr. Birtwell) and medicine (Dr. Messer), Tutts University School of Medicine, and Tutts Surgical Service (Drs. Sorott and Cloutler and Ms. Begley), and the Tutts Medical Service (Dr. Messer), Boston City Hospital, Boston, Dr. Sorott and Mr. Birtwell are now at the School of Medicine, State University of New York and Stony Brook, and the Veterans Administration Hospital, Northport, NY, Dr. Cloutier is now at the US Naval Hospital, Philadelphia. Dr. Messer is now at Rush-Presbyterian-St. Luke's Hospital, Chicago.

		MI‡						Degree		
Case No.*/Sex/ Age, yr	Hospital†	Yr Since Episode	Туре	ECG Diagnosis ‡	Poal Index	Arrhythmias or Heart Block \$	Pace- maker	of Coma, 1-4	Puimonary Disease Clinical and X-Ray Diagnosis	
Death During Assi 4/M/57	st .			Apical .	. 17	PVCs		1	Pulmonary edema	
10/F/69	В	2	IMI:	AMI	28	Atrial tachycardia	Yes	4	Vascular engorge- ment, edema	
11/M/67	С	Old	IMI	sinus tachycardia, bradycardia, arrast,			Yes	4	Congestive heart feilure, right lowe lobe pneumonia	
14/M/63	D	***		Anteroseptal	21	Ventricular fibrillation, arrest, ventricular premature beat		4	Unilateral pulmonar edema	
16/F/67	16/F/57 C Anterclateral 18 inferior		18	Right bundle-branch block, left anterior hemiblock	• • •	2	Right lower lobe in- filtrate, edema			
20/M/47	E	•••		Anteroseptal- lateral	19	Atrial and nodal tachycardia, CHB	Yes		Edema	
Death After Tempe 1/M/60	orary Hem G	odynamic i 6	Respons AMI	IMI	27	Ventricular fibriliation, ventricular tachy- cardia, atrial fibril- lation, bilateral bun- die-branch block	•••	4	Pulmonary conges- tion	
2/M/73	A	* * *		IMI	22	Bradycardia, atrial fi- brillation, PVC, nodel rhythm	Yes	1 .	Pulmonary edema	
. 9/M/66	F			iMi	. 11			+++	Lung congestion	
13/F/56	C			Anterolateral	17	CHB	Yes	. , , .	Pulmonary edema	
17/M/59	G	6	IMI	AMI	23	PAC, PVC, sinus tachy- cardia, atrial tachy- cardia	•••	2	Pulmonary edema	
Short-Term Surviv 5/M/71	ors F	Old	AMI	Apical	27	Sinus tachycardia		4	Pulmonary edema	
19/M/78.	С	•••		Anterolateral	22	PVC, ventricular tachy- cardia, arrest, bifas rhythm	Yes	4 .	Pulmonary edema	
Long-Term Survivo 3/M/51	rs F			AMI	7	· Sinus bradycardia			44.5	
6/M/54 ,	Н			Anteroseptal	19	PVC, sinus tachycardia		1	Pulmonary edema, vaacular engorge- ment	
7/M/65	block;		PVC, atrioventricular block, CHB, atrioven- tricular dissociation	Yes	ſ	Sibasilar rales				
8/M/48	F		•••	IMI	14	PVC.with bigeminy, cardiac arrests	• • •	4	+ + 4	
12/M/78	12/M/78 C Anterolateral, 22 N septal		Nodal, PVC, ventricular tachycardia, right and left bundle-branch block	Yas	•••	Rales, pulmonary congestion				
15/F/60	C	10, 9, ½	AMI	Anterolateral	27	PVC, left bundle-branch block, translent bl- fascicular block	Yes	***	Pulmonary edema	
18/M/72	1	11	MI	PMI	20		•••		Bibasilar rales, chronic obstruc- tive lung disease,	

<sup>\*</sup>Numbered in order of admission to study.

1A indicates St. Elizabeth's: B. Newton-Wellesley; C. Boston City; D. Jordan; E. Peter Bent Brigham; F. Milford; G. Cardinal Cushing General;
H. Framingham Union; I. New England Medical Center.

‡MI indicates myocardial infarction; IMI, inferior myocardial infarction; AMI, anterior myocardial infarction; PMI, posterior myocardial infarction;

tion.

SPVC Indicates premature ventricular contraction; PAC, premature strial contraction; CHB, complete heart block; bifas, bifascicular,

	Infarct to	Hours in Shock Before External	Blood Pressure, mm Ha	essure, Fluid			Urine 81		ood Gas V	alues	Central Venous Pres- sure.	Arte- rial Lac- tate,	
Case No.	Shock, hr	Counter- pulsation	With Pressors	Drug*	Hr	ml/dura-		V <sub>1</sub>	pН	Po <sub>2</sub> , mm Hg	Pco <sub>2</sub> , mm Hg	em H <sub>2</sub> O	mg/100 ml‡
,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	During Assist												
4	32	13	60/40	Lev	13	1,345/8	19	.4	7.37	48	24	20	32
10	108	2	70/40	lso Met	2	2,040/8	7	30\$	7.44	63	24	28	
11	24	9	70/58	iso Met Lev	3.5 2.5 1.5	800/8	40	0	7.45	48	41	26	48
14	5	6	75/50	Met Lev	4	1,000/8	0	0\$	7.44	35	30		45
16	Admitted in shock	12	56/40	Iso Lev	10 1	2,500/8	0	7	7.42	80	28	14	. 90
20	24	20	64/44	Lev	20	600/8	0	609	7.44	58 ·	22	101	21
	After Temporar						<del></del>	<del>,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,</del>					
1	Admitted in shock	5.75	70/54	Lev	5	500/5	14	0	7.42	110	40	11	
2	12	10	60/40	Met iso	2 10	1,150/8	19	5\$	7.40	86	45	. 15	30
9	75	13	60/40	Met	13	200/8	12	45	7.40	114	22	18	26
13	6	7	85/65	Lev	4	475/6	0	50§				28#	34
17	36	24	75/45	Met	11	870/8	2	105	7,30	38	33	14#	
	Term Survivors					···········							
5	I METITI GALLETTE	4.5	80/60	Met	2.5	2,652/8	0	409	7.20	58	42	3	44
.19	3	4	100/50	Lev	4	250/8	0	469	7.36	57	59	20	198
	erm Survivors												
3	36	24	92/70	Met Lev	23.5	1,360/10	30	10	7.38	84	38	0	13
6	7-10	14	80/60	Lev	5 <sup>-</sup> 9	930/8	30	1179	7.41	66	35	14	12
7	108	6.5	80/50	Iso	6,5	1,520/9	109	0	7.42	65	28	20	16
8	4	6	80/50	Met	5.5	560/7	0	40	7.50	55	30	10	19
12	24	6	90/60	Lev	6	645/5	0	50\$	7.33	78	40	19	15
15	5	7	80/60	Lev	7	1,425/8	0	2909	7.42	79	47	13	49
18	6	5	80/55	Met	4	1.850/16	10	129	7.25	91	38	12	26

<sup>\*</sup>Lev indicates levarterenol bitartrate; Iso, isoproterenol hydrochloride; Met, metaraminol bitartrate.

tient began to carry out the following procedures:

- 1. If necessary, a transvenous pacemaker was inserted for control of heart block. Digitalis was given if needed. Assisted ventilation through an endotracheal tube was provided if oxygenation by mask or nasal catheter proved inadequate.
- 2. Urine volume was measured hourly.
- 3. A catheter was inserted to measure central venous pressure. (In a few cases, a Swan-Ganz catheter was used to measure pulmonary artery wedge pressure.)
- 4. If the central venous pressure was below 10 cm H<sub>2</sub>O, the patient was challenged with 150-ml aliquots of

fluid over a one-hour period in an attempt to increase the preload of the left ventricle. For monitoring of arterial pressure, a polyethylene catheter (14 to 19 gauge) was inserted into a radial artery through an incision in the skin.

Arterial lactate level, pH, carbon dioxide pressure (Pco2) and oxygen pressure (Po,) were determined frequently. Metabolic acidosis was corrected with sodium bicarbonate.

When the ECP team arrived, the assist system was placed around the patient's lower limbs, and ECP was applied for up to two hours. Vasopressor therapy was discontinued as soon as possible—in most cases within 15 to 30 minutes. If the hemodynamic response during ECP was less than optimal, several measures could be taken. Fluids (5% glucose in water or lactated Ringer solution) were administered until the venous pressure rose to about 15 cm H<sub>2</sub>O. Steroids (2 gm methylprednisolone sodium succinate) were given to increase the vasodilatation, and if this was ineffective, chlorpromazine (10 mg intravenously) was given. In most patients, mephentermine sulfate (500 mg/500 ml) was slowly infused during the last 15 minutes of ECP to ensure an adequate peripheral vasomotor tone following the "assist."

If a systolic blood pressure of at least 90 mm Hg could not be maintained without vasopressors, ECP

TV is urine output (mi/hr) at time of diagnosis of shock. Vt is urine output (mi/hr) immediately preceding assist.

tNormal value for arterial lactate is 6.75-0.81 mg/100 mi.

Spatient was given a diuretic (mannitol, furosemide, or ethacrynic acid).

TPulmonary artery mean pressure (mm Hg)

<sup>\*</sup>Pulmonary capillary wedge pressure (mm Hg).

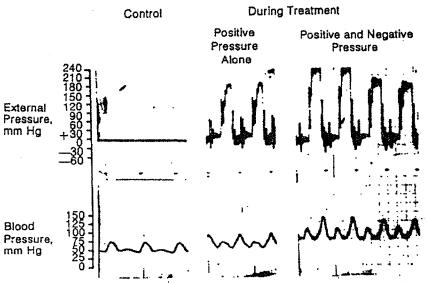


Fig 1.—improvement in hemodynamic effects of external counterpulsation with positive-negative pressure mode as compared with positive pressure alone.

was applied for additional two-hour periods until the blood pressure was stable or the patient died.

Mode of "Assist."—The ECP equipment used in this study is a self-contained, portable console that provides for monitoring of pressure and electrocardiogram. The patient remains in bed while the actuator and pressure converter are quickly placed around the lower limbs. Nondistensible seals attached to rigid, conical leg housings with hinged covers allow application of positive pressure up to 250 mm Hg and negative pressure to 150 mm Hg over the surface of the limbs

Initially, with a patient in shock, only the positive pressure pulse is used. The positive pressure is slowly increased during cardiac diastole until a maximum effect is observed on the diastolic pressure. This is usually achieved with the machine operating at a phasic pressure of 0 to 200 mm Hg.

Once the vascular bed has been actively dilated, and an adequate intravascular volume is ensured, the positive-negative mode of assist is begun. With the machine operating at pressures varying from -30 mm Hg during cardiac systole to +200 mm Hg during cardiac diastole, the hemodynamic response may be greatly improved, as illustrated in Fig 1. Of crucial importance, with either mode,

is the synchronization of the counterpulsation pump with the action of the heart."

Evaluation of Clinical Response.—
Nonsurvivors were patients who died during ECP and those who showed some response but died soon after. In the latter category were patients whose peak systolic pressure could be maintained at 90 to 100 mm Hg without vasopressors for less than 48 hours after ECP.

Patients were considered shortterm survivors if the blood pressure was normal without vasopressors for at least 48 hours, if tissue perfusion was adequate (as reflected in urine output and clinical appearance) for the same period of time, and if the ultimate cause of death was noncardiac in nature.

Patients were considered *long-term* survivors if they were eventually discharged from the hospital.

Sequential Analysis of Mortality Statistics.—To determine if ECP could be considered substantially better than current approaches to cardiogenic shock, we used a sequential design—a useful technique when the number of subjects is limited and studies must be done in a clinical setting where there is no practical possibility of having adequate controls or where the referring physicians consider a paired-control design unacceptable. A detailed explanation of sequential

analysis is given in a classic book by Wald<sup>12</sup> and in other statistical texts.

#### Result

Of the 20 patients, 9 (45%) survived—a statistically significant (P<.01) improvement over the usual 10% to 20% survival rate<sup>13</sup> (Fig 2).

To determine whether the survivors had been at less risk than the nonsurvivors before ECP, we calculated each patient's Peel Index (Table 1). This index," a prognostic tool for grading the severity of an infarct, takes into account a variety of factors that affect mortality-age, sex, history of heart disease, and immediate problems such as shock, congestive heart failure, electrocardiographic changes, and arrhythmias. Normally, a person with an index of 20 or more has less than a 25% chance of surviving. The average Peel Index of our survivors was 20, and the average of those who died was 21.

The average age of the survivors was 64 years; the average among those who died was 62 years.

There was little difference between survivors and nonsurvivors with respect to either the location of infarct or associated factors such as previous infarction. Four of the 11 patients who died and three of the nine survivors had had previous infarctions. Eight patients who died and five who survived were in deep coma when ECP was begun. X-ray films showed that almost all the patients had pulmonary edema, congestion, or areas of pneumonitis.

Arrhythmlas and Heart Block.—Eight patients who died and eight who survived (Table 1) had various forms of arrhythmias before ECP. There were four instances of partial heart block in the deaths as compared with two in the survivors, and three instances of complete heart block in the deaths as compared with one in the survivors. Five patients who died and four who survived needed pacemakers before ECP was begun.

Onset of Shock and Timing of Treatment.—The interval from the time that the diagnosis of shock was made to the start of ECP averaged ten hours for the deaths and 8½ hours for the survivors (Table 2). All the patients were given vasopressors when

Management of Cardiogenic Shock-Soroff et al

	Average	Values D	uring Extern	al Counte	pulsatio		Mean %	Pressor		ECP		
Case	Peak Systolic/ Peak Diastolic Blood Pressure,	Urine Output,	Central Venous Pressure,	Arterial Lactate, mg/	Blood	Gas V	lues	Quality	increase in Diastolic	Drugs; Steroids; Chiorpro-	Serious	Dura-
No.	mm Hg	ml/hr	cm H <sub>2</sub> O	100 ml	Hq I	Po <sub>2</sub>	Pcoz	of ECP"	Pressuret	mazine‡	Arrhythmias	min
	h During Assist			36	7.38	52	27	Fair	50			33
10	60/64 84/84	9 23	20 16		***			Fair	100	Met, iso, Mep, Lev; Metp, 2 gm; Chi, 10 gm	Atrial tachy- cardia	
11	72/64	10	30	93	7.36	57	35	Poor	5	Lev, Iso; Chi, 10 gm	Complete electrical dissociation, arrest	180
14	91/99	0		. 58	. 7,33	80	40	Good	100	Lev; Metp, 2 gm	. > >	480
16	85/90	15	14	63	7.41	133	30 .	Good -	125	Lev, Mep; Metp, 1.5 gm	• • •	480
20	98/99	95	329	30	7.53	40	29	Good	125	Dex. 4 ml	Ventricular tachycardia to asystole	
Dea 1	th After Temporary 90/110	y Hemody 8	namic Respo	ons <del>o</del>	7.41	87	38	Excel- lent	100	Metp, 2 gm	Atrial pre- mature beats	120
2	68/68 ·	12 .	. • 20	20	7.47	54	44	Fair	. 70	iso; Metp. 1.5 gm	1 to h	. 70
9	118/122	17	18	25	::-			Excel lent	300			7:
13	97/98	80	28¶	37	7.27	86	41	Good	50	Metp, 1.5 gm		120
17	95/80	.17	- * *		7.27	. 38	33	Good	77		Atrial tachy- cardia, atrial premature beats	12
She	ort-Term Survivors						20	Cand	. 50	Hyd, 3 gm		14
5	90/95 at end of ECP	68	3	54	7.39	50	32.	Good				30
19	130/155 at end of ECP	83	17	90	7.50	105	48	Excel- lent	300	Ley; Metp. 2 gm	•••	
	ng-Term Survivors	20	2	13	7.39	91	38	Good	50		• • •	11
- 3 6	112/106 112/128	. 32 76	. 11	12	7.43		34	Excel- lent	100	* **	4	15
7	115/122	55	•••	14	7.38	217	36	Excel- lent	140		*** * '	
. 8	104/107	35	15	14	7,32	85	. 35	Good	100	Met, Mep. Lev; Dex. 12 mg	Ventricular : fibriliation, arrest	. 27
12	105/106	50	15	22	7.7.7.	- 181812 <sup>18</sup>	****	Good	76	Metp, 2.5 gm.	traci	
12	92/91	35	13	• • • • • • • • • • • • • • • • • • • •	7.59	66	• 36	Good	50	. Lev, 10 min;		,20
l "	,			24	7.4		<del>7</del> 24	Good	116	Metp, 2 gm Met	*	\$1

<sup>\*</sup>ECP indicates external counterpulsation; poor, little or no increase in diastolic pressure; fair, diastolic pressure equal to systolic but no significant increase in systolic pressure; good, diastolic pressure equal to systolic plus significant increase in systolic pressure and diastolic pressure greater than systolic pressure.

\$Pulmonary artery mean pressure, mm Hg.

Thulmonary capillary wedge pressure, mm Hg.

shock was diagnosed and were on a regimen of vasopressors when ECP was begun.

Physiological Measurements.-Arterial blood pressure, taken by sphygmomanometer at the time of the diagnosis of cardiogenic shock, averaged 69/47 mm Hg in patients who died and 85/57 mm Hg in those who survived (Fig 3). The average systolic pressure of the survivors was significantly higher (P.<.001) than that of . the dying both before and during ECP. Both survivors and deaths showed similar increases in systolic pressure during the assist, but at the

time ECP was begun, the patients who died were in more profound shock than the survivors. The average diastolic pressure of the survivors was also significantly higher (P<.01) than that of the dying both before and during ECP.

Average central venous pressure

<sup>†</sup>As compared with pre-assist values.

‡Met indicates metaraminol bitartrate; iso, isoproterenol hydrochloride; Mep, mephentermine sulfate; Metp, methylprednisolone sodium succinate; Chi, chlorpromazine; Dex, dexamethasone; Lev, levarterenol bitartrate; Hyd, hydrocortisone sodium succinate.

		Vasopressors	Long-Term	Postmortem Findings
iase No.	Condition After ECP*	Given After ECP*	Follow-Up	LOPRINGE LEGISTA
	uring Assist Could not maintain blood pressure assist; cardiac arrest during intubation	Leverterenol bitartrate	*** ,	Occlusion of left anterior descending and circumflex coronary arteries; congestive heart fallure with pul- monary congestion and edema
10	Arrest following intravenous morphine sulfate	***	• • •	No autopsy
.11	Blood pressure not maintained when ECP discontinued	• • •		No autopsy  Thrombosis of left anterior descending
14	Cardiopulmonary arrest		•••	coronary artery; acute myocardiai infarction involving anterolateral walls; atelectasis, acute pulmonary edema
16	Blood pressure not maintained without ECP	Levarterenol		No autopay
20	Arrest immediately following ECP	Levarterenol Phenylephrine hydrochloride Mephentermine sulfate	•••	Old and recent occlusions of right coronary artery with myocardial inferction involving all the septum and anterior third of left ventricular wall and apex; pulmonary edema
Death /	After Temporary Hemodynamic Responsiventricular tachycardia;	isoproterenoi hydrochloride	***	No autopay
21	cardiac arrest in 45 min Hemodynamically stable. (with isoproterenol and glucagon) for 2 hr-	Isoproterenol	•••	Severe atheroscierosis of all three coronary arteries; myocardial inferction involving all the walls of the left ventricle including the interventricular septum; acute pulmonary congestion and edema
9	Stable for 2 hr, hypotension and arrest following morphine	None for 2 hr than metaraminol bitartrate		No autopay
13 <b>†</b>	Stable for 20 hr	Mephentermine for 2 hr	•••	No autopsy
17†	Stable for 10 hr	•••	•••	Severe narrowing of all vessels with old occlusion of enterior descending arteries; old, healed posterior left ventricular infarct; recent myocardial infarction involving % of septum, anterior wall, apex and lower posterio left ventricular wall; bilateral pulmonary edoma
8hort- 5	Term Survivors- Blood pressure stable at 100/70 mm Hg	. •••	Died 3 days later of peritonitis	Peritonitis, acute pencreatitis; acute anteroseptal infarction; right and left coronaries slightly narrowed but patent
19	Stable blood pressure	•••	Rémained in coma and died in third week of pulmonary edema and congestion	No autopsy
	Term Survivore Stable		Alive 12 mo	
<u>3</u>	Stable	Maphantermina	Died 8 mo later of myocardial inferction	•••
7	Stable	Mephentermine	Alive 8 mo	
8	Stable	Metaraminol bitartrate	Alive 8 mo	***
12	Stable	Mephentermine	Alive 5 mo	

<sup>\*</sup>ECP indicates external counterpulsation.
†Required ECP 24 hr after first period of assist; course of second treatment described in "Results."

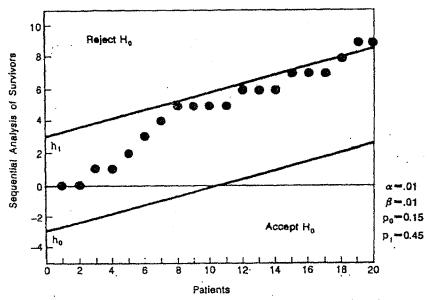


Fig 2.—Sequential analysis of clinical experience in management of patients in cardiogenic shock,  $P_o$  is the present estimated rate of survival from cardiogenic shock;  $P_o$  is the survival rate considered, on clinical grounds, to be worthwhile improvement over current rate;  $\alpha$  represents probability of erroneously rejecting external counterpulsation (ECP) as a beneficial treatment; and  $\beta$  represents probability of erroneously accepting ECP as a beneficial treatment. Line  $H_o$  marks points at which unfavorable hypothesis should be accepted (ie, there is no substantial improvement in survival rate when ECP is used). Line  $H_o$  represents points at which favorable hypothesis should be accepted (ie, ECP should be considered an improvement over standard therapeutic techniques). As each consecutive patient was treated, an appropriate point was plotted on the graph, and at each point it was decided whether to continue our study.

was 19 cm  $H_2O$  in the deaths and 14 cm  $H_2O$  in the survivors. The difference was not statistically significant. As might be expected, however, the central venous pressure of the survivors fell to 11 cm  $H_2O$  during ECP, while the average in the dying was 20 cm  $H_2O$  (P<.05).

At the time that shock was diagnosed, the urine output (V<sub>0</sub> in Table 2) averaged 10 ml/hr for those who died and 16 ml/hr for the survivors. Fluid therapy was intensified at that time, and 15 of the patients who were oliguric were given diuretics. Nine responded, and by the time ECP was begun, the average urine output (V<sub>1</sub>) was 15 ml/hr in the patients who died and 67 ml/hr in the survivors.

Biochemical Measurements,—At the time of diagnosis of shock, the average arterial lactate concentration of the patients who died was 32 mg/100 ml while that of the survivors was 15 mg/100 ml (Table 2). During ECP, as the clinical condition of the survivors improved, the lactate levels fell slightly, but in those who died the

level rose to 38 mg/100 ml (P < .05).

The pH and Po, of the arterial blood were similar in those who died and in the survivors at the time shock was diagnosed. The average Po, of the survivors increased during ECP to 95 mm Hg while in those who died it remained unchanged, but the difference was not statistically significant because of a wide scatter of the data. The Pco., however, was significantly lower in those who died than in the survivors before ECP (P < .05)perhaps reflecting a compensatory mechanism for metabolic acidosis, since the pH of the blood was similar in both groups.

Quality of Counterpulsation.—Our criteria for judging the effectiveness of ECP are given in a footnote to Table 3. In general, the hemodynamic response to counterpulsation was good even in the patients who died. The augmentation of their diastolic pressure during assist was comparable to that of the survivors (Table 3). In the deaths, the average diastolic pressure was raised only to the

level of the systolic pressure (90/89 mm Hg). In the survivors, the average blood pressure was 109/114 mm Hg during ECP.

External counterpulsation was carried out for an average of 4.4 hours in the patients who died and an average of three hours in the survivors. Three patients who died (No. 14, 16, and 20) had counterpulsation repeatedly—in one case for a total of 19 hours (Table 3). Among the survivors, the longest total period of ECP was five hours.

Course of Patients After ECP.—Table 4 summarizes each patient's condition after ECP, and the available postmortem findings in the cases of those who died.

Patients 2, 13, and 17 initially responded well to ECP, and vasopressor therapy was discontinued. However, they became hypotensive several hours later, and when ECP was reapplied for one to two hours it was not effective. They all died either during or soon after the second period of ECP

#### Comment

Patient Selection.-One question raised by any study such as this is whether the patients were representative of the general population of cardiogenic shock patients. A related question is whether there were any important differences between those who died and the survivors, as a result of unwitting biases in patient selection or variations in initial treatment. It happens that the two groups were of almost the same age range, their chances for survival, based on the Peel Index, were virtually identical, and the types of infarction were similar in both groups (Table 1). The sequence of entry into the study did not influence whether the patient lived or died, nor did it seem to matter which of the nine hospitals a patient was treated in. The hospitals include both university-affiliated and community-based institutions, some without house staff. Furthermore, the hospitals are widely scattered and therefore serve different types of patient populations in terms of socioeconomic strata and racial and ethnic origins.

Some might think that the demographic heterogeneity of the patients and the variability in initial treatment cast doubt on the validity of our data, but in our opinion these are strengthening factors since they minimized the possibility of our patients, as a group, being either unusually resistant or unusually vulnerable to the sequelae of a myocardial infarction.

Diagnosis of Cardiogenic Shock.-Another question that could be raised is whether all of our patients were truly suffering from pump failure or cardiogenic shock, and whether all standard therapeutic measures had been exhausted before ECP was tried. Tables 1 and 2 show that all the patients had indeed met the usual clinical criteria of cardiogenic shock and that every effort was made to treat them by standard procedures. Future studies in a controlled environment obviously should include measurements of cardiac output and pulmonary capillary wedge pressures as criteria for application of ECP.

The diagnosis of cardiogenic shock or pump failure covers degrees of severity ranging from mild to terminal pump failure. Although the diagnosis of cardiogenic shock was made in each case according to the criteria stated earlier, it is clear from the data that in general, the patients who did not survive were in deeper shock than those who did.

Even though the Myocardial Infarction Research Units (National Institutes of Health) have established precise, quantitative criteria for diagnosing cardiogenic shock, most hospitals are not equipped to make the necessary measurements. As a rule, physicians must base their diagnoses on clinical judgment. For example, urine volume is generally considered a good indicator of renal perfusion pressure. In our patients, urine output at the time of diagnosis of shock was 30 ml/hr or less, but many of the patients responded to diuretics and fluid-loading, so that by the time ECP was begun nine of them had a urine output of over 30 ml/hr. All of them, however, were still suffering from cardiogenic shock as evidenced by low blood pressure, need for vasopressors, clammy skin, and mental confusion.

A major problem in planning the management of patients in cardiogenic shock is the difficulty of quickly

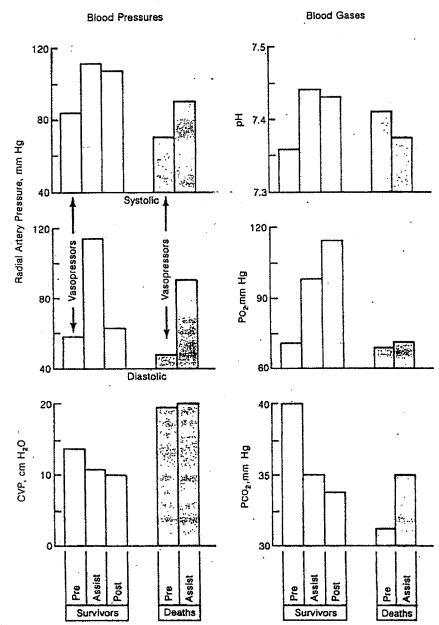


Fig 3.—Arterial blood pressure, central venous pressure (CVP), and blood gas values of 9 survivors and 11 nonsurvivors.

determining the underlying pathologic lesion. Don Michael et al," in a retrospective study of 100 patients dying of cardiogenic shock secondary to myocardial infarction, identified three subgroups whose clinical courses reflected fairly distinct abnormalities. The first subgroup (57%) had diffuse cardiac ischemia with loss of function in a major portion of the myocardium. The second subgroup (15%) had a specific and limited mechanical lesion provoking

shock. The third subgroup (28%) gave a history of a previous infarction, had cardiomegaly, and had a limited but critical infarction in an already grossly damaged ventricle. We think that early application of ECP might help to preserve myocardial function in the first and third groups by decreasing myocardial oxygen requirements and increasing the coronary collateral circulation. Experiments in our laboratory' showed that the function of an ischemic portion of the left

1448 JAMA, Sept 9, 1974 • Vol 229, No 11

Management of Cardiogenic Shock-Scroff et al

ventricle could be preserved and protected by early application of counterpulsation. In a control group, a 45-minute period of ischemia irreversibly damaged 85% of the ischemic tissue. When counterpulsation was applied during the ischemic period, only 23% of the tissue was irreversibly damaged, and when a 45-minute period of counterpulsation preceded the 45-minute occlusion, only 48% of the involved tissue was irreversibly damaged.

Timing of Application.—We believe, on the basis of our experimental data, that the sooner counterpulsation is applied after the onset of a myocardial infarction the more effective it will be in protecting the viability of the myocardium. In both the survivors and the deaths in our study, the average delay, from the time that shock was diagnosed to the time that ECP was begun, was about nine hours. Ideally, ECP should be instituted within two hours.

There is also some evidence that ECP may eventually become an important tool in prevention of myocardial infarction. In one experiment, we produced diffuse coronary occlusions by injection of microspheres into the coronary arteries. When ECP was applied before the injection, 15 of 30 animals (50%) survived, and when ECP was applied immediately after the injection, 12 of 25 animals (48%) survived, compared with only 11 of 41 (27%) in a control group. The difference was most noticeable and was statistically significant at higher doses of microspheres. Postmortem coronary angiograms suggested that the lower mortality in the counterpulsated groups was associated with the opening of collateral coronary channels. This concept is being extended to the study and treatment of patients with angina.16

Prognostic Significance of Various Measurements.—We examined the data to determine if there were any important differences between the survivors and those who died that might serve in the future selection of candidates for ECP.

At the time of the diagnosis of cardiogenic shock, the peak systolic pressure was significantly higher in the survivors than in those who died

(P<.001), and the central venous pressure was somewhat lower. Although there was little difference in urine output at the time of diagnosis, urine output in those who died did not respond to administration of fluids or diuretics and became substantially lower at the time ECP was begun. Arterial lactate concentrations and arterial blood gases were similar in both groups at the time of diagnosis.

During ECP, the rise in both systolic and diastolic pressures was significantly greater in the survivors (P<.001). Central venous pressure fell in the survivors but remained high in the patients who died (P<.05). Arterial lactate levels rose to an even higher level in those who died, but fell in the survivors (P<.05).

Effectiveness of Counterpulsation.—The effectiveness of counterpulsation can be judged by the degree of diastolic augmentation that is achieved. If the diastolic pressure can be raised to the level of the systolic pressure, it indicates that the driving pressure in the coronary vascular bed is greatly improved. Experiments have shown that the coronary vascular resistance is somewhat reduced during counterpulsation.—an indication that dormant collateral channels may be opened during counterpulsation.

Theoretically, the advantage of the external approach to assisted circulation is that the application of a positive pressure to the lower extremities during cardiac diastole causes a decrease in the transmural pressure and creates a pressure wave that is transmitted in a retrograde fashion to the root of the aorta. The release of this pressure, or the application of negative pressure, during cardiac systole causes an increase in the transmural pressure that serves to decrease the peripheral resistance. When the external pressure is zero (ie, atmospheric pressure) during cardiac systole and 150 to 200 mm Hg during cardiac diastole, the decrease in systolic pressure is only about 5 to 10 mm Hg.3 However, when a negative pressure of -25 to -50 mm Hg is applied during cardiac systole, the decrease in systolic pressure is about 25 to 30 mm Hg. In patients in shock, it is often difficult to document this decrease in the systolic pressure on a beat-by-

beat basis because the mean systolic pressure tends to increase as the patient begins to recover. The decrease in systolic pressure has, however, been well documented in normal volunteers.

There is another theoretical advantage of operating the assist device in the positive-negative mode if the patient is in profound shock. The degree to which the diastolic pressure can be augmented is limited by the volume of the arterial system of the legs. A negative pressure applied during cardiac systole tends to increase the filling of the peripheral arterial bed. With the subsequent compression of the full vascular bed during diastole, diastolic augmentation is improved.

Response of Patients to ECP .- Sequential analysis of mortality statistics indicated that the survival rate we obtained was a statistically significant improvement over the current survival rate13 in cases of cardiogenic shock. However, the sequential analysis was not designed to quantify the effectiveness of our treatment. More carefully controlled studies are needed to further characterize the types of patients for whom ECP would be most beneficial and to determine if patients who respond to ECP might survive cardiogenic shock without the assist.

Nonetheless. experience from gained to date, it is usually possible to foresee the ultimate outcome in a patient early in the course of ECP. If a patient does not respond hemodynamically to counterpulsation despite adequate fluid-loading and the use of vasodilators, the prognosis is usually grave. The response should be noticeable within 45 minutes after the start of positive-negative pressure assist and appropriate adjunctive therapy. Patients who show a dramatic response within 45 minutes—that is, elevation of diastolic pressure above the systolic level and a gradual rise of mean and peak systolic pressuresusually survive the period of pump failure. With patients who show a good but not excellent response-elevation of diastolic pressure to the level of systolic pressure and a small rise in systolic pressure—it is difficult to assess their chances for survival until several hours have elapsed. As can be seen from Table 3, some of the latter patients survived and some did not. In two patients (No. 16 and 20) ECP was prolonged to no avail. It appears to us. on the basis of our current data, that if a patient has not responded to external counterpulsation by six or at most eight hours, assisted circulation will not be adequate therapy. The only reasonable alternative, at that point, may be corrective coronary artery surgery-an approach that we believe should be reserved until assisted circulation has been tried. In patients who recover and are discharged from the hospital, longterm follow-up studies are needed to assess both their residual cardiac function and possible sequelae such as mitral insufficiency or ventricular aneurysm that are amenable to corrective surgery.

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#### Nonproprietary Names and Trademarks of Drugs

Chlorpromazine—Thorazine, Chlor-Pz, Cromedazine. Furosemida—Lasiz. Ethacrynic acid—Edecrin.

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Albert Einstein, born in Ulm, Germany, in 1879, effected the greatest revolution in scientific theory since Copernicus. He evolved his "special" theory of relativity in 1905 while he was an examiner in the patent office at Berne, Switzerland, whereas his "general" theory, involving a new concept of gravitation, was completed about 1915. Einstein's main contributions were his theory of relativity and his work related to statistical mechanics and the quantum theory of radiation.



He was appointed a professor at the University of Zurich, Switzerland, in 1909 and at the Deutsche University in Prague in 1911. In 1913, he became a professor at the University of Berlin. Later, he emigrated to the United States, where he spent the rest of his life at the Institute for Advanced Study in Princeton, NJ. He died in 1955, and his contributions paved the way for the atomic age, and are the basis for much of the medical work done with the atom.

He has been honored philatelically by Israel, Poland, Paraguay, and the United States. Israel (Scott No. 117) honored him in 1956, shortly after his death.—M. A. Shampo and R. A. Kyle

1450